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NEUROLOGY

EDITORIAL

Guest Editorial — *R. G. Lee, M.D.* 86

ARTICLES

Brain Scanning in the Detection of Tumors (Radioisotopic Encephalography) — *John R. Scarrow* 89

Increased Intracranial Pressure — *Samuel K. Silverberg* 91

Temporal Lobe Epilepsy — *Michael Shupak* 96

Remote Effects of Cancer on The Nervous System — *Chaim Shustik* 99

Clinicopathological Conference — *Rose Giammarco* 104

Grand Round Quiz — *J. P. Hooge, M.D.* 107

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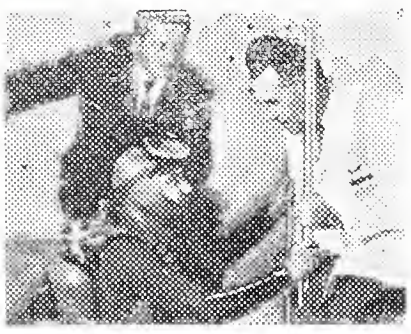

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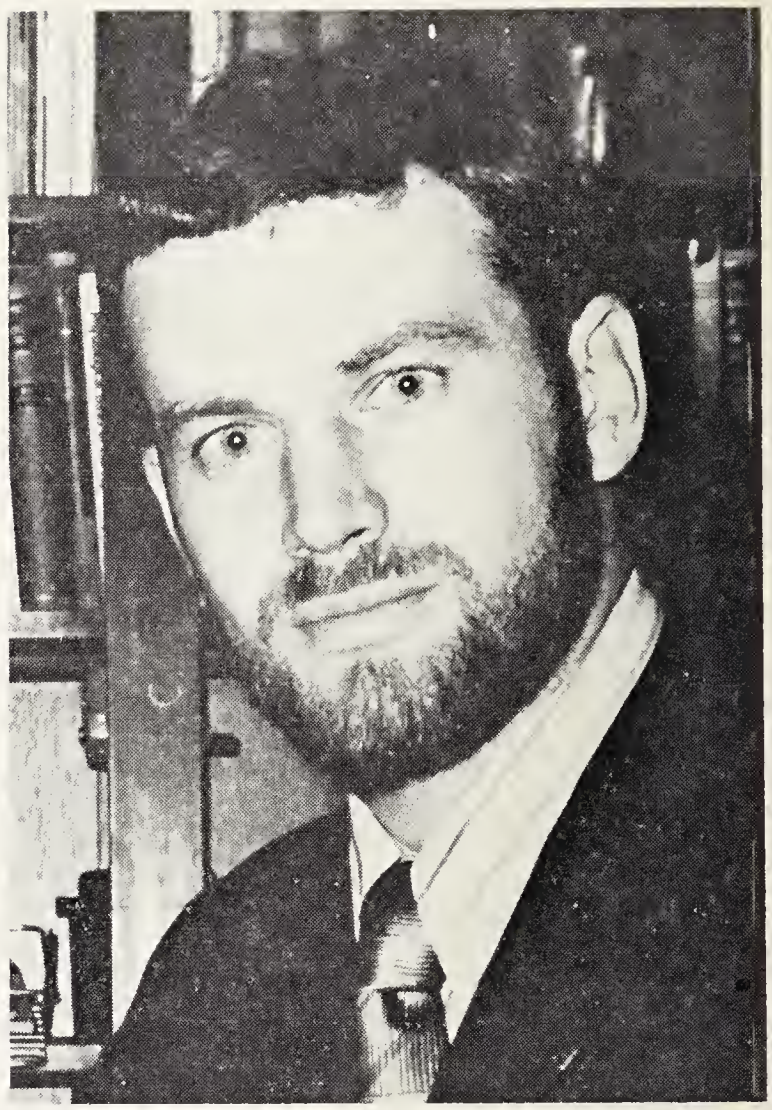
GUEST EDITORIAL

Dr. ROBERT LEE gradnated in Medicine at Toronto in 1960. After internship and two years in general practice, he took postgradnate residency in medicine at Toronto General Hospital and the Toronto Western Hospital from 1963 through 1966. He then spent two years as a fellow in Clinical Nenrophysiology at the Mayo Clinic.

F.R.C.P.(C) 1967, Dr. Lee spent a year with Dr. E. H. Lambert doing research on clinical electromyography and on experimental myopathy. He spent another year with R. G. Bickford, stndying clinical electroencephalography and the spatial distribntion of visual evoked potential, utilizing computer analysis.

He is cnrrently an Associate in the Dept. of Medicine at Toronto and Consulting Nenrologist to two hospitals — Queensway General and the Toronto Western. His research interests centre on the clinical invesitgation of epilepsy and the application of computer techniques to analysis of EEG and EMG data.

Dr. Lee will be 35 on Jnly 2, 1971.



Electrodiagnosis In Neurology

Although neurologists take pride in being able to localize and diagnose lesions in the nervous system by using simple tools and traditional clinical methods, various ancillary procedures play an important role in the investigation of neurologic disorders. Useful information can be obtained by recording electrical activity from the brain, peripheral nerves, and skeletal muscles; and electroencephalography and electromyography have become standard procedures in most neurological units.

It is almost 200 years since Galvani demonstrated the presence of electrical currents in living animal tissue, but recording these currents in a manner useful for clinical diagnosis is a relatively recent development which has paralleled the twentieth century explosion of knowledge in the field of electronic technology. The era of electrophysiology really began in the latter part of the nineteenth century with recordings from the exposed brain and nerves of experimental animals. The surgical manipulations which were required naturally precluded immediate application of these techniques to investigation of the human nervous system. However in 1929 Berger demonstrated that it was possible to record rhythmical electrical activity from the human brain with electrodes applied to the intact scalp. Although the significance of this achievement was not widely recognized for several years, it was subsequently confirmed by other investigators, and by 1940 electroencephalography was a well established procedure.

Although there is considerable variation in the normal human EEG, certain basic characteristics and dominant frequencies can be described. In most adults there is some background alpha activity (8-13 cycles per second) over the posterior head regions. This rhythm is most apparent when the brain is "idling" with the subject in a relaxed but wakeful state with the eyes closed. Alpha activity is normally suppressed by alerting the subject or having him open his eyes and it also disappears during drowsiness and sleep. Beta activity (14-30 cycles per second) is present in varying amounts, often more prominent over the anterior portions of the head. Slower rhythms in theta (4-7 cycles per second) and delta (less than 4 cycles per second) frequency ranges are not present in any significant amount in the resting EEG of the normal adult.

It is not always possible to establish a direct correlation between abnormalities in the EEG and the clinical disorder affecting the patient. Many conditions, particularly those associated with a diffuse disturbance of cerebral function, produce generalized non-specific slowing of the EEG rhythms. The EEG may look similar in such diverse disorders as metabolic encephalopathies, encephalitis, increased intracranial pressure, closed head injury, toxic states, and various diffuse degenerative conditions. However specific EEG abnormalities

which have a high correlation with certain clinical disorders do occur, and these may be of considerable diagnostic value. Persistent localized irregular delta activity strongly suggests a focal destructive lesion such as a cerebral tumour, infarct, or haematoma. Intermittent discharges of spikes or runs of rhythmical spike and slow wave activity are characteristic features of an epileptic abnormality. The EEG is often of considerable value in distinguishing between idiopathic epilepsy where the seizures are thought to most likely arise from midline sub-cortical structures and focal epilepsy arising from a localized area of cortex.

Another electrodiagnostic test which is now widely used by the neurologist is electromyography. Included under this general term are several procedures which are useful in the investigation of patients with neuromuscular disorders. Conduction velocity in peripheral nerves can be measured by stimulating the nerve electrically while recording a nerve action potential from a distal muscle. In many of the polyneuropathies there is diffuse slowing of conduction. In mononeuropathies electrical stimulation may localize the exact site of the lesion. Repetitive stimulation of peripheral nerves is used to investigate transmission across the neuromuscular junction, and this technique often helps establish the diagnosis in cases of myaesthenia gravis.

Needle electrodes are inserted directly into the muscle to record both spontaneous activity and motor unit action potentials during voluntary contraction. In normal muscle there is no spontaneous activity at rest except for brief bursts of insertion activity when the needle is moved. Abnormal spontaneous discharges such as fibrillation, fasciculation, and various types of repetitive discharges suggests pathology somewhere in the motor unit. Fibrillation potentials are of particular significance and usually indicate denervation of muscle, although they also appear in some primary muscle disorders such as polymyositis. There may also be characteristic alterations in the size and configuration of motor unit action potentials which often help distinguish between weakness of neurogenic and myopathic origin. In addition it is possible to further assess muscle function by recording the tension of contraction using a strain gauge transducer.

Two additional electrodiagnostic tests will be mentioned briefly. The electroretinogram is a complex wave form generated by the retina in response to a flash of light. It may be helpful in investigating disorders of the retina. Electronystagmography is now used in many centres to record and quantitate nystagmus and it has proven valuable for the investigation of disorders affecting the vestibular system.

In seeking further knowledge about the electrical activity of the human brain the electroencephalographer has lacked the advantage enjoyed by the electromyographer of being able to insert his electrodes directly into the tissue being studied. The formidable barrier of the intact skull and scalp severely attenuates the potentials arising from the brain, and the electroencephalographer might be compared to a person who is forced to listen to an orchestra while standing in the lobby outside the concert hall. He can detect the basic rhythms and major highlights of the symphony, but the fine details are beyond his grasp.

Since the early years of electroencephalography various techniques have been attempted to gain entry into the concert hall. In their pioneer work on epilepsy, Penfield and Jasper made extensive use of electrocortigraphy and showed that direct recording from the exposed human cerebral cortex was a valuable technique for localizing epileptic abnormalities prior to surgical excision. In more recent years a number of investigators have been making use of fine wire electrodes implanted into the depths of the human brain. These wires can be inserted with minimal risk and discomfort and can be left in place for several weeks without significant complications. This type of study has been of particular value in investigating complicated problems of temporal lobe epilepsy prior to surgery. Probing of the depths of the temporal lobes has also resulted in a common meeting place for neurology and psychiatry, and at present there is considerable interest in the possible relationship between certain types of emotional disturbance and abnormal electrical activity arising from the amygdaloid nucleus.

The wave forms recorded from the scalp represent a summation of electrical changes from thousands of underlying neurons and their processes. Our understanding of the significance of both the normal EEG and abnormal discharges has been limited by the difficulty in correlating changes in the scalp EEG with events occurring at the level of the individual neuron. The physiologic basis of the EEG is slowly becoming clearer as a result of animal experiments in which simultaneous recording has been done from the surface and from single neurons using intracellular microelectrodes. Similar recordings have been carried out in humans, recording from thalamic neurons during thalamotomy for Parkinsonism, and as the techniques of the laboratory physiologist become further adapted for clinical use, we will almost certainly see detailed studies carried out on neurons of the human cerebral cortex.

In carrying out routine visual analysis of the electroencephalogram, the physician recognizes and comments on certain specific patterns which we have described. However it has long been apparent that much of the

ongoing EEG activity is largely ignored. Undoubtedly there is much meaningful information in the signals if some method were available for extracting it, and the development of digital computers with their remarkable capacity for digesting and analyzing vast quantities of data has opened a whole new field in electroencephalography. As in many other areas, the initial attempts to apply computer techniques have probably created more new problems than they have solved. However in certain areas EEG computer techniques have now become well established. One of these is the recording of cerebral evoked responses to various forms of sensory stimulation. Under normal conditions a flash of light or a sound produces a response from the brain so small that it can barely be detected amongst the ongoing background activity. With electronic averaging techniques it is possible to summate the responses to many consecutive stimuli and obtain a clear evoked potential with a good signal to noise ratio. We are no longer limited to studying the electrical activity of the passive idling brain, and it is possible to study the brain as it is processing incoming sensory information.

With computers it has been possible to apply a variety of mathematical techniques to analysis of the electroencephalogram. Detailed studies of the frequency components present in the normal EEG and the changes which occur with altered physiologic states have been carried out. Cross correlation studies and analysis of coherence have made it possible to detect similarities in electrical activity recorded from different regions of the brain and to develop theories concerned in the transmission of information within the brain. The computer has also been used to analyze and display EEG activity in new ways which permit more accurate localization of abnormal features.

The scope of EEG is also being extended by the use of telemetry. No longer is it necessary for the subject to remain in the rather artificial environment of the EEG lab with numerous wires connected from his head to a recording instrument. Now, with compact electrode-amplifier units on the head, it is possible to record the EEG while the subject carries out his usual activities. The subject does not even need to be in the laboratory for the signal can be transmitted long distances by either radio transmission or telephone cables. These techniques have been applied to such diverse situations as recording the EEG from astronauts during space flights and monitoring spike discharges from an epileptic woman while she carries out her routine household chores.

It is clear from this brief review that, although electrodiagnostic techniques have become well established, much remains to be learned about the electrical activity of the nervous system, and particularly that arising from the brain. The complexities of the brain demand a multi-disciplinary approach with close co-operation of physicians, physiologists, mathematicians, electrical engineers, and computer scientists. It must be realized that the electrical signals are merely reflections of underlying chemical and molecular changes, and the neurochemist should be added to this list. Such an approach should provide new techniques to aid the clinician in diagnosis, and should also lead to a better understanding of complex functions of the brain such as memory, learning, and emotion. The neurologist of the future will depend on more than his reflex hammer, pin, and wisp of cotton to make a diagnosis, but at the same time he will have a clearer understanding of the complex workings of the brain than his predecessor.

R. G. Lee, M.D.

INDEX TO ADVERTISERS

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Brain Scanning In The Detection Of Tumors (*Radioisotopic Encephalography*)

John Robert Scarrow, 7T2

INTRODUCTION

The basic principle of brain scanning is that certain isotopes, when introduced into the body, will concentrate in tumors. Simply, radioactive isotopes have nuclei that are inherently unstable and decay by various modes that include the emission of α^{++}, B- or B^{+} particle and γ-ray photons from the nucleus. Since charged particles have a very limited range in tissue they are not in themselves a very useful form of detectable radiation outside the body; rather they irradiate the patient by dissipating their energy within the body and usually account for the major source of radiation to the patient. However, γ-ray photons may be detected outside the body.

SCANNERS

To produce an image of the distribution of radioactivity in a patient, a radiation detector and a recording device are required. In general, scanning systems have one or more radiation detectors, collimated so as to view at one time only a small portion of the organ being examined. A complete image is produced by moving the detector systematically over the entire organ while recording the amount of radiation at each position. There are also camera systems, where the radiation detector is stationary with respect to the organ under examination and may view the entire organ at once. Scanners, cameras, and various hybrid systems are in use today in the different hospitals and the advantages and disadvantages of one over the other will not be dealt with here.

The radioisotopic imaging systems always detect forms of photon radiation having an energy within certain limits; that is, photons with less energy than the minimum are absorbed in tissue and those with more than the maximum are not readily absorbed in the detector. At present, in radioisotopic imaging, neither scanners nor cameras produce an image with an information density approaching ordinary diagnostic x-ray systems, primarily because of the high spatial resolution of the latter. The technique is, nevertheless, of value because it provides a different kind of information which is related to organ function as well as structure.

ISOTOPES

The "ideal" substance for brain tumor localization should possess the following:

(1) a γ emitter label of suitable energy;
(2) an extremely high tumor — brain concentration ratio;
(3) a high absolute concentration in tumor tissue;
(4) a low concentration in blood because the intracerebral blood pool contributes significantly to the background activity of the normal brain;
(5) a relatively low concentration in muscle and bone;
(6) a short physical or biological half-life (*an index of the time the isotope remains in the body*) to reduce the radiation exposure.

Suffice it to say that the "ideal" isotope has yet to be found. However, of the substances that have found widespread use in man. ^{131} I – labelled serum albumin has the best ratio of [tumor] – [brain] concentrations. Unfortunately, it has the disadvantage of a high blood level. Chlormerodrin labelled with ^{203} Hg or ^{197} Hg is a popular agent for brain tumor detection in man. It has a high tumor to brain concentration ratio, and has the advantage of a relatively fast plasma clearance, compared with ^{131} I-albumin, but the disadvantage of a high renal concentration and therefore a relatively high renal radiation dose. Recently, short-lived *radionuclides*, including those eluted from generator systems, have been employed for brain tumor scanning. The most important is ^{99}mTc (technetium) eluted from the parent molybdenum, ^{99}Mo. The physical traits of the daughter ^{99}mTc are almost ideal for external detection. Since its first usage in brain tumor localization in 1963, ^{99}mTc in its chemical form of pertechnetate, has resulted in markedly improved resolution in brain tumor detection, with a shortening of procedure times.

From what has been said so far concerning scanners and isotopes, I think the point to be made is that the results of detection of the brain tumors depend greatly on the isotope used and the type of imaging system employed, and these two components must always be specified when discussing the results of detection of any specific type of tumor.

TUMOR DETECTION

The Physiological Mechanism

A differential concentration gradient occurs between a tumor and the surrounding normal brain because most substances fail to penetrate into normal brain tissue — a phenomenon described as the blood-brain barrier. In the vascular bed of tumors, this barrier breaks down and the concentration of radioactive material reaches the same order of magnitude as in other organs, such as the liver or kidney. The method of localization is, therefore, one of passive diffusion from blood plasma into tumor beds rather than a metabolic phenomenon.[1]

Using autoradiographic techniques, it was shown that with ^{131} I – albumin, the stroma of a tumor usually became

more radioactive than the parenchyma and that areas of recent necrosis were generally more radioactive than living tumor. Edematous brain was often found to be more radioactive than the adjacent tumor and cystic fluid of tumors, especially gliomas, was more active than the neoplastic tissue itself. From other experiments ^{203}Hg was shown to behave as an "intracellular substance" because its concentration in tumor was found to be independent of blood concentration.

The above experimental results along with many others not mentioned here are interesting; and although the exact why and wherefore of their occurrence is not yet known, hopefully, answers will be found and a better understanding not only of brain scanning but of the tumors themselves will follow.

SCANNING IN DETECTION OF TUMORS

The anatomical location of the brain is eminently suited to external detection methods, since there is little vascular tissue between the brain and external surface of the head except in the lower temporal areas where the vascular temporal muscles intervene. The abnormality appears as an area of high concentration of radioactivity, surrounded by a low concentration in normal brain. The radioactive agents employed thus far for the detection of intracranial abnormalities are not specific for tumors. Other organic lesions which profoundly alter the blood-brain barrier produce a similar appearance. These include intracerebral hemorrhage, edema, necrosis, abscesses, granulomas and large A-V fistulas. All of these must be considered in the differential diagnosis.

Results of scanning in evaluation of patients with suspected neoplasms must be divided into results with infratentorial neoplasms and supratentorial neoplasms; the posterior fossa tumor detection results not being as good.[2] Reports indicate that the accuracy of scanning in the detection of neoplasms in the supratentorial area is over 85%[3]. The commonest tumors — meningiomas, glioblastomas and metastatic lesions are demonstrated in a high percentage of patients (some meningiomas are missed; some glioblastomas are missed; metastatic tumors are not missed unless they are small and/or deep). Less common lesions such as low grade gliomas, colloid cysts of the third ventricle, chromophobe adenomas and cranio-pharyngiomas frequently are associated with negative scans.

Sellar and suprasellar lesions are strategically located and may first be noted clinically when they cause visual disturbances or signs of pituitary dysfunction, even though the lesions are relatively small. Furthermore, lesions in this area are hidden to some extent by pools of circulating isotope. That there is nothing about the intrinsic nature of these tumors which renders them less susceptible to detection by scanning than other lesions less strategically located can be surmised from the fact that these lesions when moderately large can be detected by the usual scanning procedures.

The low grade gliomas, however, even when they are large and located in areas that are not obscured by circulating isotope may not be associated with a large enough leak in the blood-brain barrier to be detected. Some of these tumors are solid and some are cystic and according to Feindel et al, low grade astrocytomas occasionally show a reduced counting rate compared with normal brain tissue.[4] Since not all cystic tumors are associated with negative scans, it is not the cyst itself that is responsible for a low concentration of isotope. Cysts, on the contrary, have at times been found to contain fluid with a relatively high level of radioisotope.

The fact that few meningiomas are associated with negative scans has led to the use of scanning in the differential diagnosis of bony skull lesions which might be due to a meningioma but which might also represent an are of fibrous dysplasia or an osteoma. Scanning is no doubt a valuable tool here but it is not infallible.

Glioblastomas and metastatic lesions over two centimetres in size are seldom missed on scans. Scanning has a special role in these cases. It may delineate extension of a malignant lesion across the corpus callosum better than the conventional neuroradiologic methods, and is usually superior to conventional neuroradiologic methods in demonstrating multiple lesions. For detection of small vascular metastatic lesions, angiography has the edge over scanning. Otherwise scanning is superior, for angiography in the patient with lesions not associated with abnormal vasculature reflects only vascular displacements and it is seldom possible to distinguish multiple lesions in the same area. Also one cannot postulate that a second lesion is present in order to explain "balanced" vessels in the presence of a single demonstrable avascular lesion. Furthermore, scanning often depicts the location of avascular lesions much more accurately than angiography or pneumoencephalography, which demonstrate displacement of normal intracranial structures due to a combination of tumor and edema surrounding the tumor. Thus angiography may demonstrate marked displacement of vessels near and at a distance from a small metastatic lesion while the conventional scan will show the tumor itself.

SUMMARY

Brain scanning is a valuable tool in the detection of tumors. However, it should be used only after careful neurological evaluation of the patient. Improvements in the accuracy of brain scanning are expected to grow out of research in radiopharmaceuticals and instrumentation. Real improvements in the radiopharmaceutical sphere may arise from an immunological approach (incorporation of isotope into antibody); from a biochemical approach (incorporation of isotopes with desirable physical properties into compounds selectively taken up by various brain lesions); or from the use of agents administered intravenously or intramuscularly.

(References obtainable from the Author)

Increased Intracranial Pressure

Samuel K. Silverberg, 7T1

The intracranial pressure in man is usually measured by introducing a needle into the subarachnoid space below the level of the first lumbar vertebra and connecting the needle to a glass cylinder. The perpendicular vertical height of the cerebrospinal fluid (CSF) in the cylinder is a measure of the pressure and is expressed in millimeters of water.

With the individual lying on his side on a flat surface, a height of between fifty and one hundred and eighty millimeters is considered within normal range. With the individual in the supine position, the height of the column should reach the level of the cisterna magna at about the foramen magnum of the skull. With the patient on his side, measurements above two hundred millimeters of water are considered elevated.[1]

As will be explained later, this method of measurement can be inaccurate and accompanied by a serious complication. Accordingly, there are indications and precautions for undertaking such a procedure.

For the purpose of understanding intracranial pressure, the central nervous system vault should be thought of as composed of three intracranial compartments:

1) the vascular compartment;
2) the CSF compartment;
3) the brain parenchyma.

The vascular space within the covering of the arachnoid is 100 to 150 cc. on the average. The average volume of the CSF compartment is also about 100-150 cc. It extends from the brain ventricles into the subarachnoid space surrounding both the brain and spinal cord. The brain and spinal cord comprise another 1200-1500 cc.

In the adult, the vault of the central nervous system is a relatively rigid structure. An increase in the size of any of these compartments will be accompanied by an increase in intracranial pressure (ICP), unless there is a corresponding drop in size of one or both of the other two compartments.

Under normal conditions, these compartments buffer each other against a rise in ICP. Thus a rise in intracranial blood volume will cause a seepage of CSF out of its chamber, and direct the ICP back towards normal. In an opposite fashion, gradual infusion of normal saline into the CSF space will not be accompanied by a rise in ICP. However, this buffering system tends to break down if the saline infusion exceeds a certain limiting rate.[2] The buffering system thus appears ineffective against too rapid a rise in the size of any of the intracranial compartments.

When the rise exceeds this limit and ICP rises, the expanding compartment prevents drainage of the other two compartments, thus exacerbating the pressure rise. It can be seen that above a certain rate of increase of compartment size, a vicious circle is set up to further increase ICP.

Under normal physiological conditions, the ICP increases and decreases throughout the day. A rise in intrabdominal pressure will increase the ICP by increasing the size of the intracranial vascular compartment. Normal sleep is associated with a slight rise in ICP, perhaps due to the concommitant raised blood carbon dioxide tension. The ICP also varies with each arterial pulsation and respiration. All these are either transient or very slight rises which go unnoticed in the healthy individual but which can exacerbate pathological increases in ICP.

CLASSIFICATION

It is not the purpose of this article to enumerate all the causes of raised ICP. In the April 24/69 issue of *The New England Journal Of Medicine*, there is a list of more than fifty conditions known to produce increased ICP. Interestingly, the list does not include the space-occupying lesions.

Nevertheless, the above model is useful in understanding the cause of intracranial hypertension in any disease process. One needs only investigate the effect of the disease on each of the three intracranial compartments or on the creation of an abnormal fourth compartment.

It should also be mentioned that an entity called Idiopathic Intracranial Hypertension has been described. In this case, there is no apparent cause for the rise in ICP.[3]

PATHOLOGY

The various disease processes leading to increased ICP are associated with specific intracranial pathology.

However there are non-specific pathological findings shared by those cases of intracranial hypertension due to a supratentorial increase in compartment size. These include:[4]

1) *Incisural Herniation*

Part of the hippocampal gyrus or the uncus will protrude between the edge of the tentorium cerebelli and the midbrain. This can cause aqueduct stenosis leading to supratentorial obstructive hydrocephalus. If the increase in compartment size is unilateral, the lesion is more likely on the side of the lesion.

2) *Lesion of the Third Cranial Nerve*

This nerve is flattened and hemorrhagic in the area where it passes between the posterior cerebral and superior cerebellar arteries. This is due to pressure of the

herniating hippocampal gyrus on the third nerve which is anchored in place where it pierces the dura of the skull. The lesion is more likely on the side of a unilateral expansion of compartment size.

3) *Distortion of the Brain Stem*

The brain stem is flattened in the anterior-posterior dimension by the herniating wedge of hippocampal gyrus.

4) *Injury to the Opposite Cerebral Peduncle*

The wedge of herniating brain pushes the midbrain to the opposite side, causing the opposite cerebral peduncle to be distorted by the opposite edge of the tentorium cerebelli.

5) *Hemorrhage and Ischemic Necrosis in the Midbrain and Rostral Pons*

6) *Hemorrhage and Necrosis in the Thalamus and Occipital and Temporal Lobes*

The pathology in these last two categories occurs in areas of the brain and brain stem supplied by branches of the posterior cerebral artery. The postulated mechanism is distortion of these branches by the herniating hippocampal tissue described above. This causes kinking and increased tension on these vessels, resulting in obstruction of arterioles and tearing of venules in the system.

The pathological process described above has its clinical correlation in "coning", often the terminal event of raised ICP.

A subtentorial increase in compartment size can cause an increase in ICP with its own unique pathological findings.

These include:

1) Downward Herniation of the Medulla and Cerebellar Tonsils through the Foramen Magnum
2) Traction on the Lower Cranial Nerves
3) Upward Herniation of the Cerebellar anterior lobe through the Tentorial Incisura

DIAGNOSIS

Signs and Symptoms[5]

The classic triad of increased ICP is headache, vomiting, and papilledema.

Many other signs and symptoms have been described in association with specific causes of intracranial hypertension, but these will not be elaborated on here. As well, there are a variety of non-localizing signs of raised ICP associated with various causes of this entity.

The Triad

These three signs and symptoms are found together in only half the cases of raised ICP and then, usually in the later stages.

1) *Headache*[6]

The headache of raised ICP can occur anywhere, although it is most commonly bifrontal. Slowly increasing ICP may give rise to a headache which remains level in intensity for months; or with rapidly rising ICP, the pressure may become unbearable in a few hours. Usually the headache is worse in the morning, sometimes awakening the patient. This is probably related to the increase in ICP associated with the recumbent position. Headache may be the first symptom of raised ICP as it is, for example, in 80% of posterior fossa tumors.

In summary, neither the intensity nor the location of a headache nor the absence of accompanying signs and symptoms can positively rule out increased ICP.

The cause of the headache is believed to be traction on pain-sensitive structures such as the arteries, the dura, and the cranial nerves, and changes in tension across the arterial wall.

2) *Vomiting*

The vomiting of raised ICP is often described as projectile to indicate that it is not preceded by nausea. This kind of vomiting is found most often with posterior fossa lesions irritating the medulla but may occur with other causes of raised ICP.

It should be noted that projectile vomiting is not always intracranial in origin. As well, the vomiting of raised ICP may be preceded by nausea.

3) *Papilledema*

Raised ICP is the most common cause of papilledema.

The earliest symptom of papilledema is a transient attack of blurred vision in one or both eyes.

The early signs of papilledema are hyperemia of the disc; blurring of the disc margin, particularly on the nasal aspect; dilatation of the retinal veins; and loss of venous pulsations. Later signs include elevation and reddening of the disc; increasing tortuosity of the retinal veins; flame-shaped hemorrhages; exudates extending from the disc into the retina; and contraction of the arteries.

In the early stages of papilledema, testing of the visual fields will usually reveal an enlarged blind-spot. However, macular hemorrhages can interfere with visual acuity. Prolonged papilledema will lead to a secondary optic atrophy. At this stage, the first symptom is loss of peripheral visual fields with eventual loss of central vision.

Papilledema is caused by transmission of the raised ICP to the subarachnoid space surrounding the optic nerve. This leads to obstruction of the lymphatic and venous drainages which pass through the optic nerve. This results in edema of the disc and retina.

Papilledema may be confused with optic neuritis which gives a similar fundoscopic picture. In optic neuritis, however, a marked loss of visual acuity and a central scotoma are found by simple visual testing.

Non-localizing Signs and Symptoms

The commonest symptom is diplopia from a sixth cranial nerve palsy.

Intellectual function may be impaired by raised ICP. Seizures can occur with raised ICP and often cannot be explained by a focal lesion. Decerebrate rigidity may occur as a result of effective brain-stem transection due to tentorial herniation. Stiff neck and suboccipital headache may result from coning of the cerebellar tonsils and medulla through the foramen magnum. With sudden rises in ICP, bradycardia, slowing of respiration, and a small rise in blood pressure are valuable signs. Pyramidal tract signs due to distortion of the cerebral peduncle and a fixed dilated pupil due to damage of the third cranial nerve can both result from tentorial herniation (see pathology). A general deterioration of vital signs and a decrease in the state of consciousness may represent coning at the foramen magnum and tentorial incisura respectively.

Lumbar Puncture

As described previously, inserting a needle into the lumbar subarachnoid space is a method of measuring the ICP. However, when brain ventricular fluid pressure and lumbar subarachnoid pressure have been measured simultaneously in patients with raised ICP, lower pressures have been found in the lumbar region in as many as one-fourth of cases. The mechanism postulated for this difference is a block in the subarachnoid space communication at either the tentorium cerebelli or the foramen magnum. This leads to a pressure gradient across the tentorium or foramen magnum, causing herniation of brain tissue through the tentorial incisura or the foramen magnum. (see pathology)

This mechanism is important in understanding the danger of lumbar puncture in a patient with raised ICP. If a pressure gradient has developed between supratentorial or supra-foramen magnum CSF and the CSF of the lumbar subarachnoid space, then removal of CSF from the lumbar space will increase this gradient. This enhances the possibility of brain herniation.

The cardinal symptom of coning is a decrease in the state of consciousness. In a recent series of thirty patients who had coned, 90% experienced a loss of consciousness either immediately after lumbar puncture (40%), or within twelve hours of the procedure (50%)[7]. The mortality rate with coning is high. 40% of this series died within 10 days. It is of interest then, that 50% of the series had potentially curable, non-malignant lesions before puncture.

A further point of interest is that one half of the patients in this series showed CSF pressures within normal limits by lumbar puncture measurement. This further illustrates the lack of reliability of such a measurement, and, in fact, may reflect the pressure gradient which produced herniation.

Accordingly, a number of precautions are suggested before preforming a lumbar puncture in any patient.

The emergency indications for lumbar puncture are suspicion of meningeal infection or intracranial hemorrhage, both of which are potentially curable by antibiotics or by surgical intervention respectively. When raised ICP is suspected, the procedure should be done with the patient flat on his side. A small bore needle should be used and a minimum amount of CSF should be withdrawn. The Queckenstedt test is contraindicated when raised ICP is suspected. This test requires pressing on the patient's jugular veins during lumbar puncture. If a flap-valve type of block is present at the tentorial incisura, the CSF may be forced up through the block and trapped supratentorially. This will enhance the pressure gradient and may lead to coning.

The treatment of coning is the creation of a communication between the supratentorial compartment and the atmosphere. This can be accomplished by raising a flap of bone from the skull, or by puncturing the brain ventricles and draining CSF.

RADIOLOGICAL FINDINGS

Plain X-ray

In children up to adolescence, diastasis of the sutures of the skull bones can occur in response to an increase in intracranial compartment size. This will prevent a rise in ICP.[8]

In adults and children, a chronically raised ICP is often reflected by changes in the radiological picture of the sella turcica. These include (in order of their occurrence in time):

1) Erosion of the Cortex ("lamina dura"), first seen at the base of the sella turcica at about five weeks.
2) Erosion from above of the posterior of the dorsum sellae and of the posterior clinoid processes.
3) Erosion of the bone cortex which overlies the sphenoid sinus anterior to the sella turcica.
4) Enlargement of the sella turcica.

A recent review of sellar changes showed these signs to be present in less than one-third of cases of raised ICP caused by tumors distant from the sella.[9] Other investigators have found these changes in over one-half of cases.

Another valuable plain x-ray sign, particularly in acutely raised ICP, is a shift in a calcified pineal gland. This will be caused by non-symmetrical enlargement of any of the intracranial compartments.

Radiological investigation can be of further value in diagnosing specific causes of raised ICP. Useful in this

respect are certain findings on plain x-ray, such as intracranial calcification, and the specialized techniques of brain scan, ventriculography, pneumoencephalography, and arteriography.

Electroencephalogram

It has not been well-established that there are EEG changes which are specific for raised ICP. To illustrate this fact, in a series of cases of benign intracranial hypertension (no demonstrable cause of the raised ICP), only two of sixteen cases showed EEG changes.

However, raised ICP caused by various focal lesions is often associated with generalized EEG changes. These changes cannot always be explained by the focal lesion alone.[10]

TREATMENT

Medical Management[2, 11]

Medical treatment of patients with raised ICP can be life-saving prior to, during, and after surgery. As well such treatment is of value alone when the raised ICP is the result of a process which is reverseable without surgical intervention. For example, medical treatment can be curative in idiopathic intracranial hypertension and in certain cases of cerebral edema. Medical treatment is also palliative in those with non-operative causes of increased ICP.

TREATMENT

1) *Elevation of the Head*

With freely-communicating subarachnoid space and brain ventricles, CSF pressure intracranially will fall as the head is elevated in relation to the spinal cord.

2) *Reduction of Blood Carbon Dioxide Tension*

A decrease in arterial pCO_2 will result in a decrease in cerebral blood flow, pressure and volume.

In the range of pCO_2 between 30 and 50 mm of mercury, a fall of 2 mm of mercury of pCO_2 will result in a fall of 8-10% in the cerebral blood flow. Below a pCO_2 of 30 mm of mercury, the fall in cerebral blood flow is not as marked.

In addition to this effect on blood-flow, carbon dioxide may have a direct effect on a cellular and a cell-membrane level. It is believed that the barrier to diffusion in the cell-membrane is the lipoidal layer. It has been shown that the addition of sodium or potassium to the cell-membrane lipids increases their permeability to water-soluble solutes. Carbon dioxide in the presence of bicarbonate ion would draw sodium and potassium ion from the lipid in exchange for hydrogen ion. This would decrease cell-membrane permeability and prevent glucose entry into the cells. Glycogen, fat and protein breakdown would follow with the release of products of catabolism into the cell. These water-soluble ions, trapped in the cell, would draw in water osmotically, either from the brain cell wall or from adjacent cells. Another source of intracellular water would be the water of catabolism. The result would be brain swelling and the disruption of cell architecture. It follows that reduction of brain pCO_2 would decrease intracellular water and lead to a reduction in ICP.

Too large a reduction in pCO_2, on the other hand, would result in cerebral vasoconstriction and anoxia. This becomes a danger with a pCO_2 under twenty mm of mercury.

On the basis of the above factors, a pCO_2 of thirty mm of mercury in the arterial blood is considered an optimal level for reduction of raised ICP. This can be accomplished by assisted ventilation. Tracheostomy offers the advantage of decreased anatomical dead space in the respiratory airway, and thus facilitates pCO_2 reduction. Because assisted ventilation requires positive pressure breathing, there is a tendency towards raised intrathoracic pressure and decreased venous return. This result in an exacerbation of the increased ICP by a reduction in cerebral blood drainage. For this reason, a negative end-expiratory pressure should be used.

3) *Osmotic Agents*

The use of hypertonic solutions of either mannitol, urea, or glucose intravenously has been suggested for the treatment of raised ICP. These agents act by increasing the osmotic gradient between the brain water and the blood in the brain vasculature. Thus, water is drawn from the intracellular and extracellular brain compartments. At the same time, such a mechanism should result in an increased cerebral blood flow. For ICP to fall then, the effect of decreased brain water must be greater than the effect of increased blood flow.

A rebound effect is obtained with some of these agents. About six to eighteen hours after administration, there is a rise in ICP. This is due to the entry of an agent such as urea into the brain cells and a reversal of the osmotic gradient back into the brain tissue. The effect is augmented by any factor increasing cell membrane permeability, such as mechanical trauma to the membranes. One of the osmotic agents, mannitol, remains extracellular under normal conditions and is therefore considered a more effective agent.

Because of their effect in increasing cerebral blood flow, osmotic agents are considered effective in patients with cerebral arteriosclerosis. However, in elderly patients and particularly if renal output is impaired, heart failure is a potential complication.

When intracranial bleeding is suspected, these agents should be avoided. The increased blood flow would exacerbate bleeding and the shrinking brain mass might cause tearing of subdural veins.

4) *Steroids*

Steroids of the cortisone class, such as dexamethasone, have been shown to relieve the signs and symptoms

of raised ICP. The mechanisms postulated include increased urinary output of sodium, chloride, and water; stabilization of the blood-brain barrier; and an increased binding of potassium ion to the brain cell membrane. This last mechanism is similar to the previously suggested effect of reduced pCO_2.

Of interest is the fact that raised ICP has been described in Addison's disease and after steroid withdrawal, and that both of these conditions responded to cortisone administration.[12]

Steroids with an aldosterone-like action, such as desoxycorticosterone, have been found to lack the effect of cortisone-like steroids on raised ICP, and, in fact, may aggravate this condition.

5) *Hypotension*

If the systolic blood pressure can be reduced to less than eighty mm of mercury, the autoregulatory mechanism providing a constant cerebral blood flow can, on the average, be overcome. This will result in a reduced ICP. Rapidly-acting ganglionic-blocking agents have been used in this capacity under strictly controlled conditions.

This method is of value mainly during surgery on intracranial aneurysms because of its effect in the reduction of bleeding. With prolonged hypotension, brain infarction is a potential complication, particularly in a patient with arteriosclerosis.

6) *Hypothermia*

There is no good evidence to support the use of hypothermia with raised ICP, and it may be detrimental. While hypothermia will reduce brain cell metabolism, its effect on cerebral blood flow and ICP is not clear.

SURGERY

The two basic principles of surgical treatment will be briefly noted.

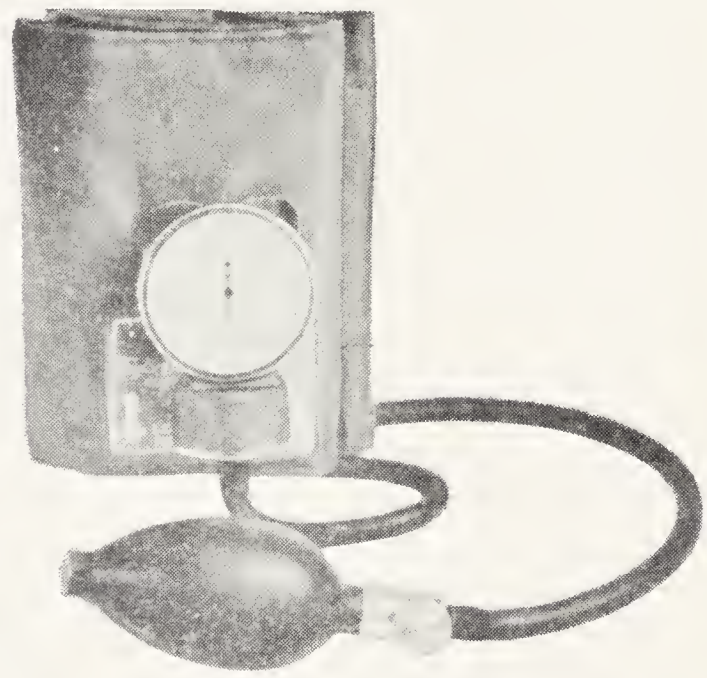
1) *Removal of Reaction Force*

This is accomplished by removal of part of the brain envelope, namely the bone of the skull vault.

2) *Removal of Action Force*

This is accomplished by surgical removal of a fourth brain compartment such as a tumor or an abcess, or by drainage of CSF, either by a shunt procedure or by direct puncture of a brain ventricle.

(References obtainable from the Author)



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Temporal Lobe Epilepsy

Michael Shupak, 7T1

Temporal Lobe Epilepsy (TLE), alternately known as Psychmotor attacks, Psychical seizures, or Automatisms is a common diagnostic problem. TLE has generated much interest in the fields of neurophysiology, psychology, psychiatry and legal medicine mainly due to its diverse and bizarre forms of expression. The varied group of symptoms may include instances of amnesia, automatism, illusion, hallucination, frank psychiatric disturbance with delusions, mania, depression and personality disorders as well as episodes of bizarre motor activity and altered consciousness. In fact, the ictal character may be obscured or nonexistent. This association of symptoms, plus (in most instances) a common temporal lobe representation, is called temporal lobe epilepsy.

The relation of TLE to other forms of convulsion may be stated simply thus: many psychomotor features may be a part of, or else precede or succeed, a generalized tonic-clonic convulsion. However, TLE and the petit mal triad (absence attacks) rarely co-exist.

Historically, seizures with automatisms (defined, according to Penfield, as moving about in a relatively normal manner, but at the same time lacking in understanding) and with complex emotional and illusory symptoms were described frequently since the time of Hippocrates; Hughlings Jackson repeatedly emphasized the post-ictal nature of automatisms depicting the feelings of familiarity and unfamiliarity (dreamy state), and associated these and the olfactory fit with lesions of the temporosphenoidal lobe (the so-called uncinate group of seizures). However, automatisms may represent an integral part of the seizure as has been since well documented.

INCIDENCE

Epilepsy in the general population is estimated at 6 to 7 per 1,000. TLE is the most frequent of all clinical forms of epilepsy ranging from 30% to 80% of epileptics in different studies; it is also the one most often accompanied by behavioural and psychiatric disorders. Estimates of institutionalized epileptics show 84% have TLE. Outpatients have the lower incidence quoted.

ETIOLOGY AND PATHOLOGY

The temporal lobe is particularly vulnerable to damage and therefore to the production of epileptogenic foci. The areas which generate psychomotor seizures include the amygdaloid nuclear complex, the pararhinal areas anteriorly (involving the posterior basal portions of the frontal lobes), and the posterior pararhinal structures, including the hippocampal gyrus and the hippocampus (Ammon's horn).

1. Herniation of the hippocampus and the medial structures of the temporal lobe (called incisural sclerosis) through the incisura of the tentorium is due to molding and compression of the infant's head during the birth process. This herniation causes ischemic changes in the temporal lobe since the anterior and posterior choroidal arteries are compressed; the result is sclerosis of the uncus, hippocampus, and part of the first temporal gyrus with varying degrees of gliosis, nerve cell destruction and small crypts. Such herniation is believed to spontaneously reduce itself. The term "medial temporal sclerosis" was introduced because the nerve cell loss and gliosis were not limited to Ammon's horn, but extended diffusely to involve amygdala and other parts of the hippocampus and temporal lobe. Medial temporal sclerosis appears to be related only to epilepsy of infancy and early childhood; in epileptic adults this lesion was not found if the epileptogenic process was initiated by a lesion after infancy.

2. In infancy, anoxia from any cause, hypoglycemia, febrile convulsions or an episode of status epilepticus may readily effect damage of the temporal lobes.

3. Acceleration – deceleration (contre-coup) head injuries damage the inferior aspect of the temporal lobe near the sphenoidal wing.

4. Space-occupying lesions such as neoplasms, infarcts, hamartomas or vascular malformations involving the medial temporal lobe have greater epileptogenic potentiality than similar lesions elsewhere.

5. Infection from middle ear and mastoid may spread to the temporal lobes.

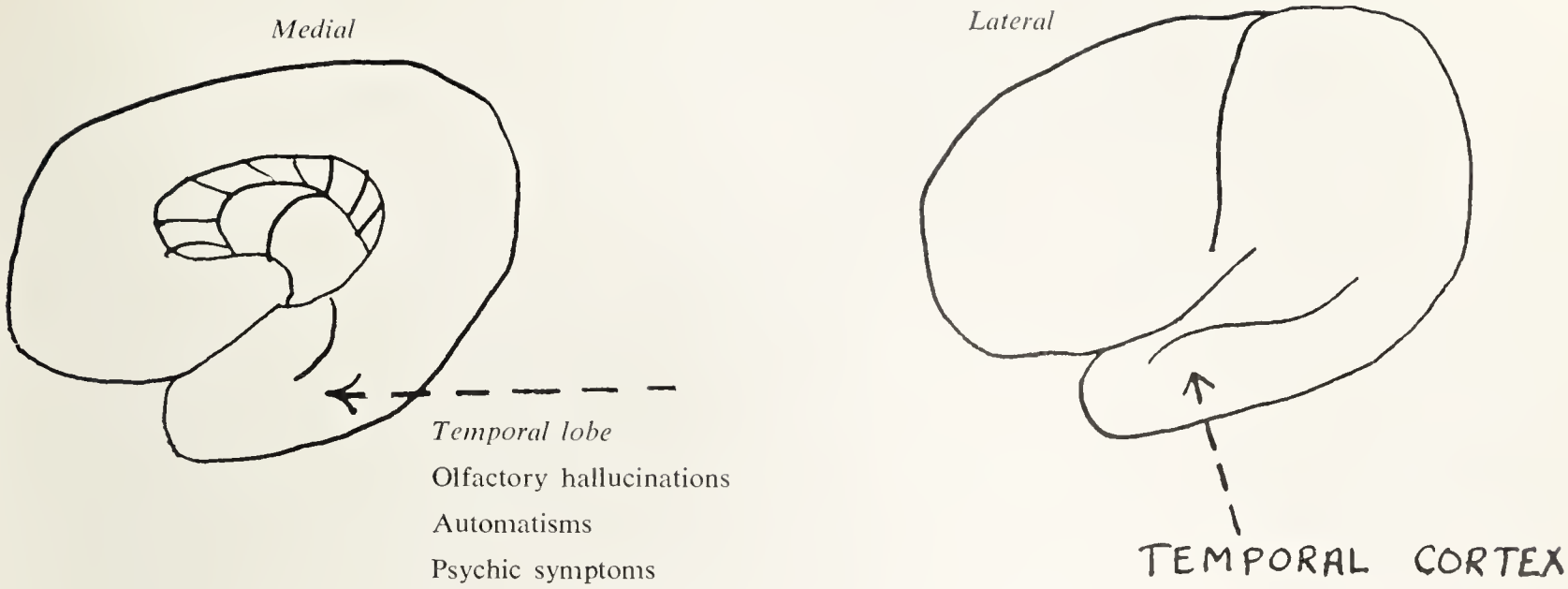
6. Genetic predisposition, as evidenced by family history.

7. Rarely a distant lesion may trigger TLE.

The hippocampal area has the lowest seizure threshold of any cortical area. The locations of lesions in TLE, in order of decreasing frequency, are hippocampal, focal temporal cortex and diencephalic. In summation, TLE should be regarded as a cryptogenic disturbance and not idiopathic.

GENESIS OF CLINICAL FEATURES

To the anatomist's description of the temporal lobe as that part of the brain which lies below the Sylvian fissure and which blends posteriorly with the occipital lobe, the clinician would include the hippocampal region, which involves the hippocampal gyrus with the uncus, the hippocampus and the amygdala. These structures have connections with the insula and the entire limbic system. The neurophysiology of these structures are beyond the scope of this review, but a simplified diagram follows:



Temporal lobe
Olfactory hallucinations
Automatisms
Psychic symptoms

Anterior temporal	*Sylvian*	*Mid-temporal*	*Posterior temporal*
Psychic symptoms	Epigastric sensations	Auditory hallucinations	Visual hallucinations
Deja vu	Facial movements	Vertigo	Dreamy state
Automatisms	Dreamy state	Depression	Depression
	Automatisms	Deja vu	
	Taste hallucinations	Depersonalization	

Ref.: Sutherland.

CLINICAL PRESENTATIONS

The multiple manifestations of TLE can be divided into three major categories: sensory, motor and psychical.

A. *Sensory:* The patient may complain of sensations which are extroceptive (gustatory, olfactory, auditory, vertiginous, visual or somatesthetic) or introceptive (oropharyngeal, esophageal, abdominal, retrosternal or a feeling of asphyxia). These symptoms if present alone would pose difficulty in diagnosing TLE, unless one is familiar with the patient's personality and can rule out organic illness elsewhere.

B. *Motor:* These include simple or complex abnormal movements, autonomic or speech disturbances.

C. *Psyche:* Automatisms are common and these are distinguished from frontal automatisms by their lack of stereotyped thinking or behaviour and by the presence of phychic aura and dreamy states. There is an increased incidence of functional psychiatric disorders between TLE episodes. One study of 300 patients with TLE showed severe personality disturbance in 42%, with undiagnosed psychoses in 6% and suicidal attempts, schizophrenia, manic-depressive psychoses to a lesser degree. These patients tend to be aggressive and hostile. Other studies have arrived at lower figures.

The personality changes in an epileptic are attributed to both the disease process itself and to adaptive phenomena. The changes described (Brown) are slowing of mental processes with the inability to concentrate and circumstantiality, loss of adaptability, prolongation of affect, and perseveration. Late changes are loss of discrimination in the use of words, with deficiency of ideas, egocentricity, preoccupation with body and health, and hypersensitivity and aggressiveness.

The reaction of the epileptic to his illness is influenced by his premorbid personality. Conflicts with his peers and society are constantly arising from childhood through marriage and into adulthood. Behaviour may be controlled by momentary moods. Some of the paradoxical personality changes noted are obstinacy and abnormal sensitivity, grandiosity and submissiveness, politeness and outbursts of profanity — all in one patient.

DIAGNOSIS

TLE can be suspected if several of the above-mentioned clinical features are elicited from a patient's history or from a relative. If a convulsion has taken place, an accurate description, any localizing features, and post-ictal phenomena are to be noted. Clinical examination of the suspected epileptic includes his general appearance and a complete physical and neurological examination. Ancillary investigations are blood work (glucose, calcium, urea, and serology), x-rays of the skull and chest, electroencephalography (EEG) and radio-isotope brain scanning.

The EEG must be interpreted in context with other clinical findings. It is possible that a patient may have a completely normal EEG and yet have well-documented clinical seizures. Single records obtained from patients

with TLE may be normal in as many as 30 to 40 per cent of patients; this proportion is reduced if the EEG is examined during sleep and if multiple records are obtained. Also, an abnormal EEG may be shown by patients with no history of seizures or any neurological illness.

Temporal lobe seizures are not accompanied by the EEG pattern of spikes, although for some hours or minutes beforehand the localized spike discharge may be obvious. An interseizure pattern of abnormal brain wave activity is present in a high proportion of epileptic patients. These can be enhanced by various activation techniques — hyperventilation, photic stimulation, and sleep recording (induced or spontaneous). When the temporal lobe seizure starts, low voltage fast rhythms are commonly seen, commencing in the area where the spike was seen previously. These rhythms often spread widely to involve the whole of one or both hemispheres and they frequently are followed by a generalized discharge consisting of rhythmic slow waves with a frequency of 6 c.p.s. and a flat top as the convulsion progresses. It has subsequently been found that a variety of different EEG patterns may also be seen during the ictus (in contrast to the above classical description by Gibbs and Lennox). If there is no major seizure, there is usually little or no post-ictal flattening of the EEG. Lesions of the temporal lobe are frequently responsible for major convulsions, which are the result of spread of the electrical discharge from the lesion to deep thalamic regions and then to all brain areas. In contrast, motor or sensory cortex lesions are less frequently responsible for grand mal attacks, being more often associated with the focal motor or sensory seizures not accompanied by loss of consciousness.

The EEG has many limitations in determining the location and etiology of a cerebral lesion. Skull x-rays are usually non-contributory in TLE. Brain scans depend on the localized breakdown of the blood brain barrier. An increased isotope uptake in the temporal area provides substantial evidence of pathology. Echoencephalograms are safe and simple tests for detecting shift in midline structures. If indications exist, further investigations should be done: carotid angiography, pneumoencephalography, and ventriculography. Prior to ordering these tests, one must balance the high risk of the procedure and the information that they can provide.

MANAGEMENT OF TLE

A patient presenting with a history indicative of temporal lobe epilepsy must be adequately assessed and diagnosed and the underlying pathology determined. Thereafter, the general principles of epilepsy management are followed. These include:

A. Treatment of a generalized seizure with gentle restraint and an open airway.

B. General and social implications: This is a complex matter on account of lay ignorance and superstitious beliefs regarding epilepsy to the point where it is socially unacceptable and causes rejection. TLE may correlate with aggressive or otherwise disturbed behaviour and epileptics in general have a higher incidence of intellectual and personality disorders. The epileptic should be reasured that controlled convulsions do not lead to mental or intellectual deterioration; and, he should lead a normal life with only certain common-sense restrictions.

C. Anticonvulsant therapy: The choice drugs recommended for TLE are diphenylhydantoin (Dilantin) and primidone (Mysoline), alone or in combination. A significant control can be achieved in 50 to 60 per cent of patients on average doses of diphenylhydantoin 100 mg tablets three times daily and/or primidone 250 mg tablets, two to three times daily. Newer compounds which have been of benefit in controlling temporal lobe seizures (as well as other focal seizures) include carbamazapine (Tegretal). Side-effects of these drugs are common and may necessitate discontinuing or altering therapy.

D. Neurosurgery: Temporal lobectomy (excision of anterior and medial part of one temporal lobe including the uncus, amygdala and the hippocampus) is considered if seizures occur despite anti-convulsant therapy and a unilateral temporal lobe is involved. Helpful information can be obtained by using sphenoidal and nasopharyngeal leads during EEG studies and also with depth electrode implantation and electrocorticography. A pneumoencephalogram may demonstrate temporal lobe atrophy or an expanding lesion involving the temporal lobe and a unilateral angiogram may demonstrate a meningioma, vascular malformation or other space-occupying lesion.

Complications that may arise from TLE include hemiparesis and visual field defect, and if the dominant hemisphere is involved, dysphasia and auditory agnosia. For patients incapacitated by uncontrolled seizures or whose behavioural disorders associated with TLE necessitate institutional care, the risk of a complication may be entertained.

Temporal lobotomy (the section of nerve fibre tracts in one or both temporal lobes without removal of tissue) has been attempted to control the mental state of TLE patients. However, little beneficial effect upon the psychosis, affective change or personality disorder has been reported.

SUMMARY

Temporal lobe epilepsy is a common disorder that is often overlooked or misdiagnosed on account of its multiple manifestations. Positive clinical and investigative data and a degree of suspicion in psychiatric and hysterical patients can result in the control of seizures and abnormal behaviour with drugs or surgery in the majorit yof cases. *(Continued on page 103)*

Remote Effects Of Cancer On The Nervous System

Chaim Shustik, 7T1

INTRODUCTION

When neurological complications in patients with carcinoma were first described, the nature of the association with neoplasm was not appreciated, the intercurrence being regarded as fortuitous. In the past few decades reports from different investigators have given statistical significance to the relation and impressively distinct clinical syndromes have been identified as occuring with particular neoplasms.

It is difficult, however, to establish a consistent perspective on these conditions. Carcinomatous neuromyopathy has achieved a respectable status in the differential diagnosis of peripheral neuropathy. Other conditions are exceedingly rare and if seen would warrant the attention of editors of neurology journals.

It is important to appreciate that the patient presenting with certain neurological symptoms and signs may be harbouring a malignancy in the absence of any other findings and with specific recognizable syndromes, the diagnosis may be reasonably ascertained.

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

The neurological uniformity and the relative frequency of lymphoproliferative disease (chronic lymphocytic leukemia and malignant lymphomas) as a background to this neurological disorder is well documented. The name was originally applied to a unique affection of the brain occurring in the course of Hodgkin's disease and lymphoma.

Pathology: This is a distinct neuropathological entity because it shows features which do not occur in any other disorder. The lesions are characterized by multiple foci of demyelination widely disseminated throughout the CNS with total disappearance of myelin sheaths with relative preservation of axis cylinders. In addition to demyelinating lesions which don't have predominantly perivascular distribution, changes in oligodendrocytes are constant. These consist of enlargement of their nuclei with dense basophilia and loss of nuclear detail. An interesting finding is the occasional demonstration of eosinophilic intranuclear inclusions within these abnormal oligodendrocytes.

Clinical Features: The disease occurs in a setting of longstanding chronic disease and pursues a relentlessly progressive course from onset to death being on the average about 3 - 4 months.

The neurological symptoms and signs vary greatly corresponding to the widespread dissemination. Hemiparesis is frequent, often evolving to quadriparesis in the terminal phases. Some degree of dementia is noted almost invariably. Visual field defects are common and even blindness may occur. Cerebellar dysfunction may be reflected in abnormalities of gait.

Investigative procedures to establish a neurologic diagnosis are usually negative except for the EEG which is consistently abnormal with non-specific diffuse and asymmetrical slow wave activity. The results are predictable from the character of the process which although affecting the brain diffusely, is in general unaccompanied by the phenomena of inflammation and doesn't produce space-occupying lesions.

Etiology: Although progressive multifocal leukoencephalopathy is being reported with increased frequency, the etiology of this condition is still a subject of speculation. A favoured hypothesis suggests that the condition is the result of viral infection of the CNS in patients with immune impairment occurring in the presence of certain kinds of pre-existing chronic disease as evidenced by the frequent association with malignant lymphomas. In these diseases, impairment of immune responses, particularly of delayed type, has been repeatedly demonstrated.

The changes in the oligodendrocytic and astrocytic nuclei are consistent with the cytopathologic effects of a virus reinforced by evidence of abnormal accumulations of DNA in the affected nuclei. The atypicality of the lesion could be the result of a defective immune response since the absence of an inflammatory reaction is one of the noteworthy features.

DIFFUSE POLIOENCEPHALOPATHY

Various clinical syndromes from amyotrophic lateral sclerosis to dementia have been described in association with neoplasm and these diverse clinical entities have been classified under the general heading of polioencephalopathies. The pathological evidence suggests that these entities are actually parts of a spectrum although the patient will present with symptoms indicative of predominant involvement at a certain level of the CNS.

The initial symptoms may consist of a wide range of psychiatric disorders for which the patient would in some probability be admitted to a mental hospital. There may be a simple dementia which is fairly rapid and progressive, or a disorder of memory with or without confusion and disorientation. Symptoms of mood disorder are frequently encountered such as depression, anxiety and agitation. Psychiatric symptoms may or may not be associated with symptoms and signs of focal cerebral disease.

Subacute Cerebellar Degeneration is a form of encephalopathy and a syndrome on which attention has been focused because of the striking rapidly evolving picture it produces although the number of cases reported in the literature is rather limited.

Pathologically, the lesion is characterized by diffuse loss of Purkinje cells in the cerebellum. In addition degeneration of the long tracts of the spinal cord has been observed, most commonly and most usually advanced in the direct spinocerebellar tract.

Clinically, in relating the syndrome to type and site of neoplasm, carcinoma of the ovary and of the lung seem to predominate. In a series by Brain, the neurological symptoms antedated the symptoms of the tumour in 10 of 17 patients, in 1 case appearing 3 years before. Cerebellar degeneration commonly presented as unsteadiness and difficulty in walking, and in most of the cases marked dysarthria was present as well. Nystagmus is not a prominent symptom but may be present. The final depressing picture is therefore one of a person, previously in apparent good health, now unable to walk, feed himself or speak intelligibly.

Superimposed on this may be symptoms of muscular weakness due to associated degeneration of motor ganglion cells of either cranial or spinal nuclei. Thus ptosis, opthalmoplegia, facial and palatal weakness have been noted to occur as well as wasting and weakness of limbs with diminution or loss of tendon reflexes.

Thus despite the distinctive pathological changes in the cerebellum, clinically the damage is not usually entirely limited to the cerebellum. Brain raises the intriguing possibility that the remarkabie parallel between subacute cerebellar degeneration and the hereditary disease, scrapie, in sheep may suggest a genetic factor operative in the production of this syndrome.

CARCINOMATOUS MYELOPATHY

The spinal cord changes complicating carcinoma are of two types. Mention has been made previously of one type in association with subacute cerebellar degeneration in which there may be systematized degeneration of certain fibre tracts especially the direct spinocerebellar tract. In these cases, the gray matter of the spinal cord was intact, in distinction to the other type of carcinomatous myelopathy. The sensory roots were also intact so that degeneration of the dorsal columns was not a secondary phenomenon.

Those patients with spinal cord involvement, in addition to the predominant neurologic symptoms referrable to the cerebellum, show asymmetrical tendon reflexes. Extensor plantar responses, sensory abnormalities mediated by involved columns and varying degrees of motor weakness of upper motor neuron type are also seen.

The second type of carcinomatous myelopathy is characterized by a progressive ascending sensorimotor deficit inovlving the legs and trunk and occasionally the arms. The rapidly progressive nature of the disorder is seen in its abrupt onset with fatal termination in days or weeks. Of the cases described in the medical literature males and females are equally affected with most over 40 years of age at time of onset. Carcinoma of the lung is the most frequent reported neoplasm and the time of onset of symptoms and discovery of the neoplasm are variable.

The earliest neurological signs were impairment of strength and sensation in the legs and sphinctor disturbances, which evolved rapidly, implicating successively ascending segments of the trunk. Lower motor neuron involvement is established by the flaccid, arreflexic paralysis of the limbs.

The pathologic lesion is characterized by the striking degree of tissue destruction in the spinal cord most severely the thoracic region with indiscriminate involvement of gray and white matter.

Considering the clinical and pathological features, this syndrome has been called "subacute necrotic myelopathy."

NEUROPATHY

When considered as neuromyopathies, combined muscle and nerve lesions, this group constitutes the most frequently reported remote effect of carcinoma. In carcinomatous neuromyopathy, the nervous system may be effected at several different levels in the same patient and the muscles may also be involved. Although precise classification is difficult, several groups have been recognized. Studies by Croft and Wilkinson concentrated on carcinoma of the lung and of the breast and showed that 16% of 250 men with carcinoma of the lung and 4.4% of 250 women with carcinoma of the breast demonstrated neurologic abnormalities compatible with neuromyopathy.

The types of neuromyopathy seen were:

1. Neuromuscular disorders. These were the commonest (in 80% of male series, 45% of female series) and the type most commonly missed. The term neuromuscular disorder is used for its convenience since it is not always possible on clinical grounds alone to distinguish minor manifestations of a lower motor neurone lesion from minor degrees of a myopathy and frequently there are no neurological symptoms. The most common difficulty is in walking or going upstairs which is casually attributed to general cachexia or non-specific effects of the neoplasm. The commonest abnormality is diminution and/or loss of tendon reflexes. In addition, a noteworthy point in examination is the difference in power between the proximal and distal muscles, the latter being normal. Proximal weakness may be manifest in inability to lift the legs off the bed yet normal dorsiflexion of the

feet is present. The disorder is characterized by progressive unremitting weakness of proximal muscle groups.

2. Polyneuritis. The next most common form is the polyneuritic type, seen in 12% of the patients with neuromyopathy in the study. In this type, a mixed motor and sensory loss is the clinical picture.
3. The other types of neuropathy occur infrequently and often in combination with each other such as sensory neuropathy, cerebellar, motor neurone, and myasthenic pictures.

Croft and Wilkinison found evidence of neuromyopathy in 7% of all cases of cancer reviewed.

Carcinomatous neuromyopathy may occur with many types of neoplasm although it is more likely to occur in patients with carcinoma of the lung, ovary or stomach. In women with carcinoma of the breast, the incidence of neuromyopathy was only 4.4%.

From their analysis, there was little to suggest that the incidence of carcinomatous neuromyopathy is affected by the age of the patient, the length of time the patient has had symptoms of the cancer, the blood group or the amount of weight lost.

In carcinoma of the breast, where the incidence of neuromyopathy is low, previous treatment does not seem to alter the incidence of neuromyopathy whereas in carcinoma of the lung in men, neuromyopathy is commoner when the carcinoma has been treated surgically or by radiotherapy.

In lung carcinoma, the histological type of tumour does not seem to have any relation to the incidence except that the incidence is lower in patients with undifferentiated carcinoma.

Sensory peripheral neuropathy is another disorder which seems to be limited to carcinoma of the lung. The pathology is a degeneration of posterior root ganglion cells and/or nerve fibers with which a selective demyeliination of the dorsal columns of the cord may be associated. Clinically, this may appear as a progressive loss of all forms of sensibility which tends to extend gradually over the whole body in association with sensory ataxia and diminution or loss of tendon reflexes. Deafness may occur and in a proportion of cases there iis also dysesthesia and pain.

It must be emphasized that a pure sensory neuropathy is extremely rare and most patients with sensory loss also show symptoms of associated lower motor neuron lesions, due to peripheral nerve degeneration.

MUSCULAR DISORDERS ASSOCIATED WITH NEOPLASMS

Myasthenic State and Lung Carcinoma

In the early studies of neuropathy and myopathy associated with carcinoma, it was apparent that some patients with these disorders had muscle weakness with easy fatiguability resembling that of myasthenia gravis. An occasional patient had, in addition, transient diplopia or ptosis. The neoplasm in patients who had these symptoms and signs suggesting a defect of neuromuscular transmission almost invariably was a carcinoma of the bronchus, usually of small cell or oat cell type.

Lambert and Eaton have studied this syndrome most extensively and it has been variously called "atypical myasthenia gravis", "pseudomyasthenia" and "myasthenic-myopathic syndrome" but most often the "myasthenic syndrome".

Clinical Features: Myasthenic syndrome occurred predominantly in men over 40 years of age (mean 59 years). Initial symptoms as well as the major complaint in almost all patients was weakness and easy fatiguability of legs. As is often the case, weakness was usually first noticed in getting up from a chair or in climbing stairs.

In general, symptoms of impairment of muscles innervated by cranial nerves were relatively infrequent and mild in degree (ptosis, diplopia, mild difficiulty in swallowing). The weakness of the proximal muscles of the extremities especially of the pelvic girdle and thighs was demonstrable by neurological examination. Careful testing in both weak and strong muscles usually revealed an appreciable delay in development of strength at the onset of a maximum voluntary contraction, requiring an evident interval of seconds to develop maximal force. As in myasthenia, weakness developed earlier in prolonged exertion. Muscle wasting is not a prominent feature of the syndrome and by itself cannot account for the findings. Tendon reflexes may be found to be weak or absent particularly in the lower extremities. Laboratory inivestigations have failed to demonstrate any pertinent abnormalities and muscle biopsy has only shown non-specific alterations in the minority of cases.

The most decisive information for identifying the myasthenic syndrome is provided by the response of a muscle to maximal electrical stimulation of its nerve in electromyographic studies. The principal features of the defect in neuromuscular transmission have been a marked block of transmission in rested muscle but a marked facilitation in active muscle.

Lambert and Eaton concluded that the facilitation of muscular contraction is not the result of progressive recruitment of motor units but results from the progressive increase in the number of active muscle fibers within the motor unit. The proposed site of dysfunction is the neuromuscular junction and by analogy with the similar defects produced by botulinum toxin and magnesium, the release of acetylcholine at the nerve ending is implicated as the predominantly impaired mechanism.

Although no casual relationship between the carcinoma and the defect of neuromuscular transmission has been demonstrated, in some instances temporary recov-

ery does occur following therapy, compared with no remissions in the absence of therapy (in Lambert's series) and the possibility of a humoral factor has been suggested to account for the association.

Differentiation of the myasthenic syndrome from classical myasthenia gravis is possible by clinical and EMG findings. In contrast to the rarity of ocular and bulbar involvement in myasthenic syndrome, such symptoms often predominate in myasthenia. Easy fatiguability characterizes the muscle weakness in myasthenia, whereas in the myasthenic syndrome an initial gradual increase in strength occurs. Other features of the myasthenic syndrome such as diminished or absent muscle reflexes, aching of muscle, dryness of the mouth, paresthesias and loss of potentia are not usually associated with myasthenia. In myasthenic syndrome, all muscles tested, whether weak or strong clinically, had an easily-demonstrable, marked defect or neuromuscular transmission by EMG. The response to a single, maximal nerve stimulation was greatly reduced in amplitude as compared to a normal response in myasthenia, but the amplitude of action potentials evoked by tetanic nerve stimulation increased in height.

Another means of distinguishing the two disorders is the difference in the effect of Decamethonium. Although small doses may cause transient improvement of neuromuscular transmission in some muscles in both conditions, on administration of large doses patients with the myasthenic syndrome developed more profound weakness than normal persons while patients with myasthenia are generally less sensitive to the drug than normals.

Abnormal sensitivity to muscle relaxants is present in both conditions e.g. increased sensitivity to tubocurarine, and prolonged apnea following administration during surgical procedures may be the first clue to a defect of neuromuscular transmission.

Guanidine which increases the amount of acetylcholine released by the nerve impulse has been more effective in managing myasthenic syndrome than the anti-chloinesterases, neostigmine and edrophonium.

Neoplasms and Muscle Disease

Although the association of dermatomyositis with malignant tumours had been noted earlier, it was in 1954 in a paper by Henson, Russell and Wilkinson that the concept of "carcinomatous myopathy" was introduced and thereafter included in the differential diagnosis of muscle disease appearing in adult life.

Despite attempts to equate carcinomatous myopathy with polymyositis and even dermatomyositis, the absence of significant interstitial cellular infiltration in the histological picture of the former gives rise to some skepticism about the validity of the assumption. Without any implication of pathogenetic mechanism the term "carcinomatous myopathy" is an operational description of muscle disease in a patient with no rash, when a tumour is present and other causes of myopathy are absent.

Pathology

In a series of 25 patients by Silverstein and Shy, all of which had myopathic changes and 18 of which had neuropathic changes, the pathological changes were interesting for the lack of inflammation present. This corroborated the evidence of Henson, Russell and Wilkinson who considered that the muscle changes found viz. variable degree of atrophy and necrosis of individual fibres, lacked specificity and were disproportionately slight in relation to the observed clinical disability.

Shy considered that the changes are suggestive of a cellular change within the muscle cell but cytochemical studies had not revealed which component of the muscle cell is first involved in the disorder.

Clinical

As mentioned previously it is often difficult to differentiate the neuropathic from the myopathic component in a patient with proximal muscle weakness where both may overlap. Indeed, the histological changes at autopsy may suggest carcinomatous myopathy whereas the clinical picture may have been primarily that of neuropathy.

For this reason, documentation of cases is rather controversial, and frequently the term "neuromyopathy" is used to encompass all the cases. The incidence of neuromyopathy associated with carcinoma has been quoted earlier from Croft and Wilkinson.

Conversely, in a series of 131 cases of late myopathies studied by Shy, cancer was found in 18.3% and in patients over 50, in 39%. Sex differentiation after 50 is interesting when cancer is found in 71% of the men and 24% of women.

There is no uniformity in the time sequence of appearance of the myopathy with relation to the diagnosis of carcinoma. In Shy's series of 25, 18 had the myopathy preceding the findings of carcinoma, in the remaining 7, the carcinoma occurred before the myopathy presented. The two disorders may occur within one month to five years of each other.

The onset is usually insidious. The picture is that of progressive unremitting weakness of the large proximal muscles associated with atrophy with sparing of the more distal musculature. In certain cases, weakness of the trunk muscles may be prominent with consequent spinal deformities and abnormalities of gait.

The tendon reflexes are diminished or lost in the areas affected by the weakness and the absence of fasciculation is suggestive of a purely myopathic nature for the disorder.

The observation was made that in some patients with carcinomatous myopathy the appearance of the tongue is highly characteristic being smooth, and redder than usual and not changing in appearance on administration of the B vitamins.

Carcinomatous myopathy is not uniquely associated with any type of tumour but has been described with carcinomata of the lung, breast, prostrate, thyroid, rectum, cervix and with lymphomas.

There has been no correlation between the extent of the symptomatology and the size of the tumour.

This disorder, finally, must be differentiated from the weakness seen in a generally cachectic patient for it is a specific response of marked weakness of striated muscle in the absence of cachexia.

GENERAL CONSIDERATIONS

It is a difficult proposition to create a semblage of order from the bewildering array of neurological signs and symptoms which may be associated with the presence of a neoplasm elsewhere in the body. With the present state of knowledge the most convenient and orderly approach is to classify the complications on a clinical basis, which has been attempted. Pathologically, the changes associated with the clinical syndromes are diverse and there is no evidence to suggest a common pathogenetic mechanism operative in the production of those changes.

The clues pointing to certain etiological mechanisms have been discussed in some cases, but no definitive casual relationships have been established. There is speculation about the role of other mechanisms in the neurological syndromes, some suggested by analogy with other neurological conditions and some by disturbances known to be produced by neoplasms.

The endocrine-metabolic syndromes associated with malignancies and the identification of humoral agents supposedly elaborated by neoplasms exerting biologic affects stimulated investigation for possible humoral agents. Although insight has been gained into the metabolic abnormalities produced by neoplasms there is little evidence to implicate alterations in neural metabolism caused by humoral factors. Thus, aside from neurological abnormalities associated with eg. hypercalcemia (PTH-like substance), Cushing's (ACTH-like material), hypoglycemia (insulin-like material) in which other findings are also present, no role for a hormonally mediated mechanism has yet been substantiated.

Studies on the systemic effects of tumours have demonstrated abnormalities in lipid and protein metabolism. Observed depletion of fat in tumour bearing mice and human patients raises the possibility of catabolic effects on structural lipids in the CNS by tumours, resulting in nervous impairment.

In view of the well known effects of nutritional deficiency on the nervous system, it was logical to consider its possible role in effects of carcinoma on the nervous system. However, in comparing the effects on different parts of the nervous system, there is little clinical or pathological similarity between the nutritional and carcinomatous polyneuropathy in adequately nourished individuals and its clinical progression despite oral and parenteral administration of all known vitamins. In addition, the peripheral nerve is limited in its response to varying noxious insults, so that these similarities don't indicate a common etiology.

Finally, as in all other poorly understood pathologic conditions, immunologic etiology presents an inviting avenue to explore. There is abundant evidence from studies in tumour immunology that most cancer cells are endowed with specific antigens capable of arousing a cytotoxic immune response in their hosts. Extrapolating from this, it is possible to construct a thesis of common antigens shared by tumour cells and nervous system elements with resulting cross reactivity producing nervous lesions.

SUMMARY

This paper has dealt with neurologic manifestations of neoplastic disease essentially by reviewing those aspects which have been described and observed by clinicians, and on occasion confirmed by pathologists. But aside from the recognition of an existing association, the challenge remains to answer most of the questions which present themselves. What are the mechanisms underlying the production of these diverse syndromes? Why are certain symptoms associated only with special types of neoplasm? Further insight into the nature of cancer may permit finer resolution of detail.

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(Continued from page 98)

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CLINICOPATHOLOGICAL CONFERENCE

Post-Traumatic Seizures In A 57-year Old Man

Rose Giammarco, 7T1

On the night of Oct. 5, 1970, a 57-year-old business man, with no previous medical history or complaints, tripped and fell, hitting his head on a cement sidewalk. He lost consciousness for approximately one hour. He was examined in the emergency department within two hours of his fall. Except for a left posterior superficial scalp abrasion, no abnormalities were found on examination. Skull X-rays and neurological examination were normal, and the patient was sent home.

That same night, the patient experienced severe pain in his left ear and felt as if he was going deaf in that ear. During the night, he observed a watery, yellow-coloured discharge from his left ear.

There was no history of previous ear problems.

Two days later (1 p.m., Oct. 7/70), the patient was found unconscious in his room, having apparently had a generalized seizure. He was unconscious, breathing heavily, slightly cyanotic, and with evidence of urinary incontinence. A half-hour prior to this, he had been alert and speaking to a friend on the phone.

There was no history of epilepsy or of any other seizure in the past.

The patient was immediately brought to the Montreal General Hospital and was examined in the emergency department. At that time, he was drowsy but oriented to time, place and person. He did not remember anything of his seizure.

The temperature was 103°F, the pulse 80, blood pressure 100/60, WBC — 18,000.

Physical examination was normal except for a moderately stiff neck (and fever). Neurological examination at that time was within normal limits: cranial nerves intact, no focal signs; reflexes, power, tone and co-ordination were all within normal limits.

Immediately after being examined, the patient suddenly began having a focal seizure, which began with clonic movements of the right arm, progressed to the right half of the face, the right leg and subsequently progressed to a generalized seizure. The patient became cyanotic, unconscious, and incontinent of urine. An airway was established and the patient was sent up to the Neurology ward.

A lumbar puncture was done to rule out meningitis (the patient had fever, leukocytosis, and stiff neck). The opening pressure was 150 mm, cell count — 370 rbc, 29 lymphocytes, 7 polys; glucose 84, protein 130. The CSF results for culture and sensitivity, acid-fast bacilli and VDRL were all negative.

A more thorough examination on the ward that evening revealed the following:

Bulging of the left tympanic membrane (bluish-red in colour) with no evidence of perforation. No mastoid tenderness or swelling was present. There was moderate neck stiffness on flexion. The oral temperature was 103°F. The patient was alert, oriented, coherent in his speech. Cranial nerve examination revealed a decreased corneal reflex on the left, a nuclear Left VII lesion and a supranuclear Right VII lesion. The other cranial nerves were normal.

There was a right hemiparesis (arm and leg), and decreased sensation of pinprick in the right arm and hand. Reflexes were slightly increased on the right arm and leg, with a questionable extensor plantar on the right. Position, vibration and co-ordination senses were within normal limits.

Skull and left mastoid films were negative. A diagnosis was made of septic corticothrombophlebitis secondary to a fracture of the left petrous temporal bone. As such a fracture is extremely difficult to detect by radiological examination, the diagnosis was made on the basis of the history of head trauma followed by L. ear pain, transient deafness, and discharge of fluid. The diagnosis is further strengthened by the finding of left nuclear VII nerve and L. corneal involvement, contralateral hemiparesis, and the CSF analysis results. The CSF increased protein, increased cell count (moderate), but *normal* sugar indicate infection close to, but not in, the subarachnoid space.

Using septic (2° to petrous fracture) corticothrombophlebitis as a working diagnosis, the plan was to start the patient on high doses of anticonvulsants and high doses of antibiotics, since septic corticothrombophlebitis is an extremely epileptogenic lesion.

Immediately prior to starting medication, the patient went into *status epilepticus*, each seizure beginning with clonic movements of the right arm and progressing to a generalized seizure. The patient had 3 generalized seizures within 20 minutes.

The following medications were given: Valium — 10 mgm. i.v. *stat* for the status. Dilantin — 100 mgm i.m. *stat* to be followed by 100 mgm *q.i.d. i.m.* Phenobarbital

— 300 mgm *i.m. stat* with 60 mgm *t.i.d. i.m.* Ampicillin — 12 gm/day in *i.v.* fluid.

The following day (Oct. 8), the patient was much better. His temperature was 100°F. Lumbar puncture results were: opening pressure 170 mm; cells — 50 rbc, 4 lymphocytes, 1 polymorph. (Glucose and protein — not done).

The patient had no further seizures while in hospital.

The patient continued to improve over the next few days. He still had a mild R. hemiparesis and L. VII nuclear lesion. However, he complained of a persistent Left sided headache. Daily fundoscopic examinations were normal until Oct. 21/70 when a slightly blurred Left disc was noted.

SUMMARY OF INVESTIGATIONS:

A. – X-rays: Skulls (including basal views) mastoid films were repeatedly normal:
Oct. 7, 8, 14, 22. No pineal shift.

B. – Lumbar punctures (as stated in preceding discussion).
Oct. 16. Opening P. 200 mm CSF. Cells — 2 lymph. Protein 60. Glucose 70.

C. – Brain Scans (Technetium Brain Perfusion & Scan):
Oct. 13, 15, 20 — Repeatedly normal.
Oct. 22 — Radionucleotide.
Cerebroangiogram following angiography was *normal. No* abnormalities to suggest a space-occupying lesion.

D. – Echograms — Oct. 7, 14, 19 — normal. *No* shift.

E. – EEG's — showed serially deteriorating EEG patterns:

1) Oct. 8 — No epileptogenic activity. Focal area of cortical dysfunction in L. precentral hemisphere.

2) Oct. 13 — Extensive area of cerebral damage, L. centro-temporal with spread to frontal.

3) Oct. 20 — bifrontal slow waves. Considerable abnormality in L. anterior head region.

F. – Angiogram — On Oct. 22, 1970, a left carotid angiogram was done because of symptoms and signs pointing to a L. space-occupying lesion. Before angiography, the differential diagnosis was cerebral abscess, intracerebral hematoma or subdural hematoma. The left angiogram showed a 6-7 mm shift of vessels from left to right, across the midline *plus* a small subdural collection of fluid. A relatively avascular area (4x3 cm.) was seen in the central region in the upper convexity. No pathological vessels were seen.

G. – Post infusion brain scan — normal.

CLINICAL EVOLUTION

On Oct. 23 the Optic Discs were blurred bilaterally. There was a slight R. hemiparesis (R. arm drift). A definite extensor plantar reflex was elicited on the right.

Oct. 23-26: The patient was still complaining of L. sided headache; showing increasing clumsiness of his right hand and had occasional episodes of inappropriate affect and responses. No dysphasia was observed.

NEUROSURGERY:

Oct. 27: A Ventriculogram was performed through a L. parietal Burr hole. This showed the whole ventricular system (except the 4th ventricle) deviated to the Right. A 6-7 mm shift of the *septum pellucidum* to Right was clearly demonstrated. A small subdural collection of fluid (15 c.c.) was evacuated but this subdural collection was not enough to account for the large shift noted on angiography and ventriculography.

Exploration was repeated on Oct. 29 when a large left posterior parietal hematoma (intracerebral) was evacuated. More than 30 cc of blood was obtained. Culture and sensitivity, and cytological studies done on the evacuated specimen were negative.

Subsequently the patient did well, improving steadily during the remainder of his stay in hospital.

A brain scan was done on Nov. 5 with the following results:

1. A Flow study showed no significant difference in hemispheric perfusion and no localized areas of abnormal vascularity.

2. The delayed 1 hour scan showed an elongated peripheral area of increased activity in the Left temporal-parietal area (posterior). This was thought to be due to a local healing process following damage to the brain.

DISCUSSION

One of the presenting problems in this man was focal seizures. These are always siignificant, and suggest a focal lesion. Trauma may cause such seizures immediately after the injury (within hours or days) but this is very rare, especially for a non-penetrating head injury. (The average interval between a severe head injury and the first seizure is approximately 9 months.)

A cerebral tumor (especially one close to excitable motor cortex) or an Arterio-Venous Malformation may give rise to a focal seizure. However, trauma, tumor, and vascular malformations very rarely, *if ever*, give rise to *status epilepticus* of the grand mal convulsive type. A septic venous thrombosis, however, pro-

duces a highly epileptogenic focus which can often progress to grand mal status.

The foregoing generalities can now be applied to this case. Because of the history, the cranial nerve findings (compatible with a petrous temporal fracture) and the CSF findings, it is likely that the original symptoms and findings were the direct results of a septic cortico-thrombophlebitis.

The basis of the aural discharge could have been better clarified by glucose analysis of the fluid, and by culture. Had this fluid been available for examination, one could distinguish between a CSF leak with petrous fracture, and otitis media. Since no discharge was present on the patient's admission to hospital, the watery, yellow-tinged fluid discharge was assumed to be CSF leak, probably blood tinged. This is compatible with the cranial nerve findings secondary to a petrous fracture.

Status epilepticus (with grand mal convulsive status) is a life-threatening situation, and unless terminated naturally or by treatment, death ensues due to asphyxia, circulatory collapse and hyperthermia. Severe and continuing convulsions are frequent complications of acute disease processes affecting the brain.

Intravenous diazepam (Valium) was used in this case to terminate the status condition. It is not useful for general control of seizures and therefore Diphenylhydantoin (Dilantin) and Phenobarbital were also started to prevent further seizures.

The question still remains as to whether this patient's large intracerebral hematoma was the direct result of trauma, or whether he had a pre-existing vascular malformation which bled, or a tumor (unlikely) which bled, the bleeding being precipitated by trauma.

With the type of injury sustained by this patient, the posterior parietal location of the hematoma is unusual. One would expect the hematoma to be further anterior, i.e. temporal or antero-parietal in location. It is also unusual in an adult, except in geriatric patients, to have such a large hematoma with no skull fracture. Thus the possibility exists that the patient had a pre-existing asymptomatic A-V malformation which bled consequent to minor trauma.

It was important to rule out a cerebral abscess in this case. Although rare, *unrecognized* progression of infection to brain abscess frequently leads to death. It should also be remembered that fever and leukocytosis in the presence of an intracerebral catastrophe do not always indicate infection. A reaction to irritation, e.g. blood in the CSF, will produce a similar picture.

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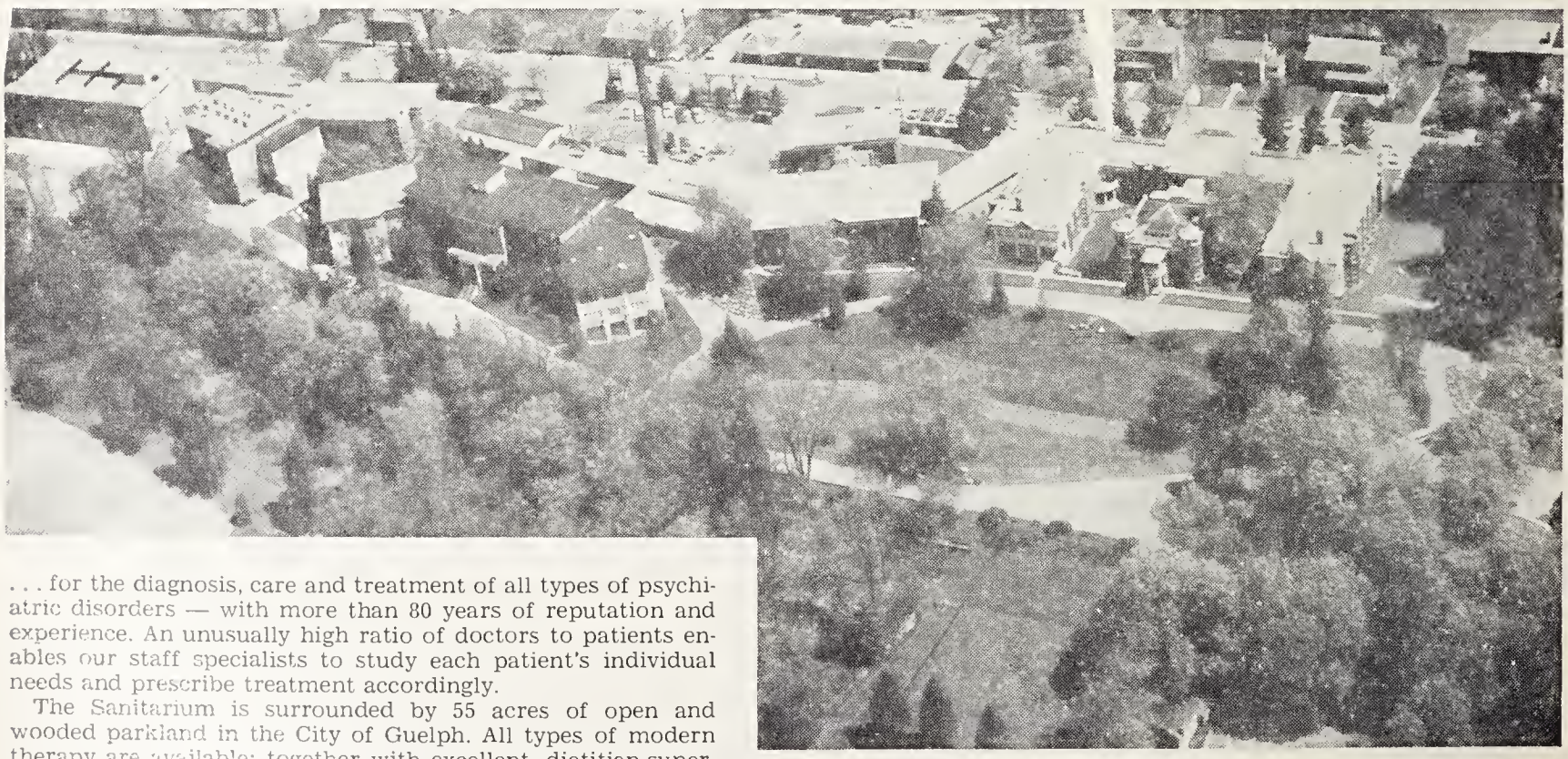

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Grand Round Quiz: Neurology

J. P. HOOGE, M.D.
Assistant Resident in Medicine
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1. *Fatal Middle Cerebral Artery Infarction causes a picture consisting of:*
   (a) Contralateral hemiplegia, hemianaesthesia and homonymous hemianopsia
   (b) Ipsilateral hemiplegia, hemianaesthesia and homonymous hemianopsia
   (c) Ipsilateral hemiplegia, hemianaesthesia and bi-temporal hemianopsia
   (d) None of the above.

2. *In a patient with a stroke, bilaterality of Neurological abnormalities suggests:*
   (a) Involvement of carotid system
   (b) Involvement of basilar system
   (c) Middle cerebral artery disease
   (d) Cardiac disease
   (e) None of the above

3. *The following are manifestations of Parkinson's Disease* EXCEPT:
   (a) Lack of facial expression
   (b) Rest tremor
   (c) Flaccidity
   (d) Slowness of movement
   (e) Stooped posture

4. *Frequent findings in cerebral palsy are:*
   (a) Scissor's gait
   (b) Athetosis
   (c) Spastic Paralysis
   (d) Mental Retardation
   (e) All of the above

5. *Multiple Sclerosis is commonly manifested by all of the following* EXCEPT:
   (a) Weakness
   (b) Sphincter and gait disturbances
   (c) Visual disturbance
   (d) Abnormal reflexes
   (e) Headaches

6. *Wernicke's disease is characterized by all of the following* EXCEPT:
   (a) Nystagmus
   (b) Bilateral sixth nerve palsy
   (c) Papilloedema
   (d) Ataxia
   (e) Apathetic personality

7. *Cardinal signs of craniopharyngioma include all of the following* EXCEPT:
   (a) Increased intracranial pressure
   (b) Visual defects
   (c) Speech defects
   (d) Endocrine dysfunction
   (e) Hypothalamic dysfunction

8. *In Myasthemia Gravis:*
   (a) The tensilon test is rarely used
   (b) Facial muscles are frequently affected
   (c) Ocular muscle fatiguability appears late
   (d) All of the above
   (e) None of the above

9. *In Multiple Sclerosis:*
   (a) Trauma is an important casual factor
   (b) Infections and operations may be followed by onset of the nervous symptoms
   (c) There is a greater incidence in tropical than temperate countries
   (d) All of the above
   (e) None of the above

10. *A patient suddenly feels dizzy, vomits and has dysphagia. On examination he has a Horner's syndrome plus analgesia and thermo-anaesthesia on one side of the face with similar sensory deficits on the opposite side of the body. He most likely has suffered:*
    (a) Thrombosis of the anterior cerebral or middle cerebral artery
    (b) Thrombosis of the posterior inferior cerebellar artery or vertebral artery
    (c) Hemorrhage into the internal capsule
    (d) Embolism of the posterior cerebral artery
    (e) Occlusion of one corotid artery

11. *In the Argyll-Robertson pupil:*
    (a) Mydriasis is present
    (b) Reaction to mydriatics is prompt
    (c) Reaction to light is prompt
    (d) Reaction to convergence is prompt
    (e) All of the above

12. *If both jaw jerk and arm jerk are very exaggerated the lesion is usually:*
    (a) Just below the foramen magnum
    (b) At the foramen magnum
    (c) In the medulla
    (d) Below the pons
    (e) Above the pons

13. *The most common sciatic nerve lesion:*
    (a) Is disc disease of one or more of its roots?
    (b) Occurs as part of the Guillain-Barre syndrome
    (c) Involves the knee jerk but spares the ankle jerk
    (d) All of the above
    (e) None of the above

14. *Polyneuropathy:*
    (a) Usually produces a symmetrical spastic paresis
    (b) Usually does not alter sensory functions
    (c) Usually affects proximal more than distal segments of limbs
    (d) All of the above
    (e) None of the above

15. *Korsakoff's Psychosis:*
    (a) Is characterized by loss of memory for recent events plus confabulation
    (b) Is rarely associated with disorientation in time and space

(c) Is infrequently due to alcoholism
(d) All of the above
(e) None of the above

16. *The most important "false" localizing sign of intracranial tumor is:*
(a) Hemiplegia
(b) Homonymous hemianopsia
(c) Oculomotor palsy
(d) Abducens palsy
(e) Mydriasis

17. *The Neurologic manifestations of early bacterial meningitis include:*
(a) Stiff neck
(b) Kernig and Brudzinski signs
(c) Photophobia
(d) All of the above
(e) None of the above

18. *All of the following are postulated mechanisms of headache* EXCEPT:
(a) Dysfunction of extracranial arteries
(b) Traction on intracranial vessels
(c) Pressure on cranial nerves
(d) Pressure on cerebral parenchyma
(e) Cervical spondylosis

19. *The primary source of infection in pneumococcal meningitis is often:*
(a) Compound skull fracture
(b) Otitis media or sinusitis
(c) Pneumonia
(d) Any of these
(e) None of these

20. *Ruptured Intracranial aneurysm frequently presents with:*
(a) Severe headache
(b) Nausea and vomiting
(c) Loss of consciousness
(d) Nuchal rigidity
(e) All of these

Answers

1 — A

The middle cerebral artery through its superficial and penetrating branches supplies a large area of brain including parts of the frontal, parietal and temporal lobes, and also parts of the basal ganglia and internal capsule. The classical picture of fatal superficial and deep middle cerebral infarction is contralateral hemiplegia, hemianaesthesia and homonymous hemianopia. If the dominant hemisphere is involved global or total sensori-motor aphasis is also present.

2 — B

The basilar artery and its branches supply the brain stem. In the brain stem tracts descending to and ascending from each side of the body either cross each other or run in close proximity, in contrast to the cerebral hemispheres where the motor and sensory tracts subserving the two sides of the body are distantly separated. Other signs of brain stem disease include nuclear or infranuclear involvement of one or more cranial nerves, vertigo, diplopia, cerebellar ataxia, Horner's syndrome and deafness.

3 — C

Manifestations of Parkinson's disease can be grouped into (1) Rest tremor (2) Akinesia or Bradykinesia (3) Rigidity (4) Loss of Postural Reflexes. In the second group are seen poverty of spontaneous movement, loss of normal associated movements, and slowness in the initiation and execution of all voluntary movements.

4 — E

Cerebral palsy is a term that embraces a large number of diseases different etiologically and anatomically. There is primarily a major disturbance of motor function, usually non-progressive, and present since infancy or childhood. Two major types are the spastic type and the choreo-athethoid type. Mental function may be normal, superior or retarded. Birth injury has been involved as a leading cause of this disease.

5 — E

The symptoms of multiple sclerosis are varied depending on the site of the plaques of demylination. Weakness and abnormal reflexes are very common and usually indicate corticospinal tract involvement. Retrobulbar neuritis producing sudden loss of vision in one eye or diplopia is another common presenting symptom. Many patients lose control of sphincters secondary to spinal cord involvement. Headache is not a common symptom.

6 — C

Wernicke's Disease is most commonly seen in the alcoholic who is rationally deficient. The cardinal manifestations are bilateral sixth nerve palsy, nystagmus, various conjugate gaze palsies and ataxia. Usually these manifestations precede the mental changes (primarily apathy, listlessness and confusion), by 1 to 2 weeks. This disease is a true neurologic emergency and is treated with I.M. or I.V. thiamine. If left untreated, the mental changes are usually irreversible.

7 — C

Craniopharyngiomas usually lie above the sella turcica, depressing the optic chiasma and extending up into the third ventricle. In this position they can produce hypothalamic and endocrine dysfunction and classically a bitemporal hemionopia. They can cause increased intracranial pressure by virtue of acting as a space occupying lesion and obstructing CSF flow. They are not typically located near speech areas and therefore do not cause speech defects.

8 — E

Myasthenia Gravis is a disease characterized by weakness and easy fatigability. It most frequently affects facial, oculomotor, laryngeal, pharyngeal and respiratory muscles. Diplopia, due to unequal weakness of the ocular muscles, is usually the first symptom. Myasthenic fatigability can be demonstrated by having the patient make some repetitive or sustained movement and can be promptly reversed with the I.V. administration of tensilon.

9 — B

Symptoms of multiple sclerosis are commonly precipitated by infections, operations, vaccination, and pregnancy. It is a common disease in temperate climates and rare in tropical countries.

10 — B

The symptom complex described is that of the lateral medullary syndrome. Although occlusion of the posterior inferior cerebellar artery is usually stated as the cause, this is probably not so in more than 20% of cases, the other 80% being secondary to occlusion of the vertebral artery. Other symptoms which may occur in this syndrome are ataxia and falling to the side of the lesion, nystagmus, loss of taste and hiccups. The syndrome is produced by infarction of a small wedge of lateral medulla.

11 — D

The Argyll-Robertson pupil is classically found in neuro-syphilis. The pupils are usually small, irregular and unequal. They fail to react to light but do constrict on accommodation. They do not dilate properly in response to mydriatic drugs. There is still controversy about the site of the lesion in the Argyll-Robertson pupil. Some place it in the tectum of the midbrain and others in the ciliary ganglion.

12 — E

The jaw jerk is a reflex mediated by the fifth cranial nerve (more significantly via the mesencephalic nucleus of the fifth). Since the fifth nerve emerges from the lateral border of the pons and the mesencephalic nucleus extends further cephalad, a lesion below the level will not be associated with an exaggerated jaw-jerk.

13 — A

Disc disease is by far the commonest cause of sciatic nerve compression. Most lumbar herniations occur between the fourth and fifth lumbar and first sacral bodies compressing L_5 and S_1 nerve roots respectively. The ankle jerk is mediated by S_1 and the knee jerk by L_4.

14 — E

Polyneuropathy is an impairment of function of many peripheral nerves simultaneously, resulting in a symmetrical distribution of flaccid muscular weakness, and usually also of sensory disturbances, affecting as a rule the distal more than proximal segments of limbs, and sometimes also affecting the cranial nerves. Polyneuropathy has a large number of causes, can be acute, subacute or chronic and can present with primarily sensory, motor or combined symptoms.

15 — A

Korsakoff's psychosis is a disorder of mental function in which retentative memory is impaired out of all proportion to other cognitive functions. There is a persistent inability to acquire new information and skills. As a rule, patients with this disorder have only limited insight into their disability, and tend to be very apathetic and inert. Confabulation is found frequently but is not found in all patients with this disorder. The most common cause is alcoholism with nutritional deficiency.

16 — D

Commonly *Abducens* palsy is seen in cases where intracranial pressure is increased when the pathologic process, particularly a tumor, does not affect the nerve directly. This paralysis has been assumed to be due to the stretching of the nerve and occurs when the brain is dislocated somewhat. However, it may be due to traction on the nerve exerted by the anterior inferior cerebellar artery which as a rule runs just above it.

17 — D

Photophobia, stiff neck, and Kernig and Brudzinski signs are all important indications of early meningitis. Also important are mental changes, commonly delirium in the early stages, with drowsiness, stupor and coma later.

18 — D

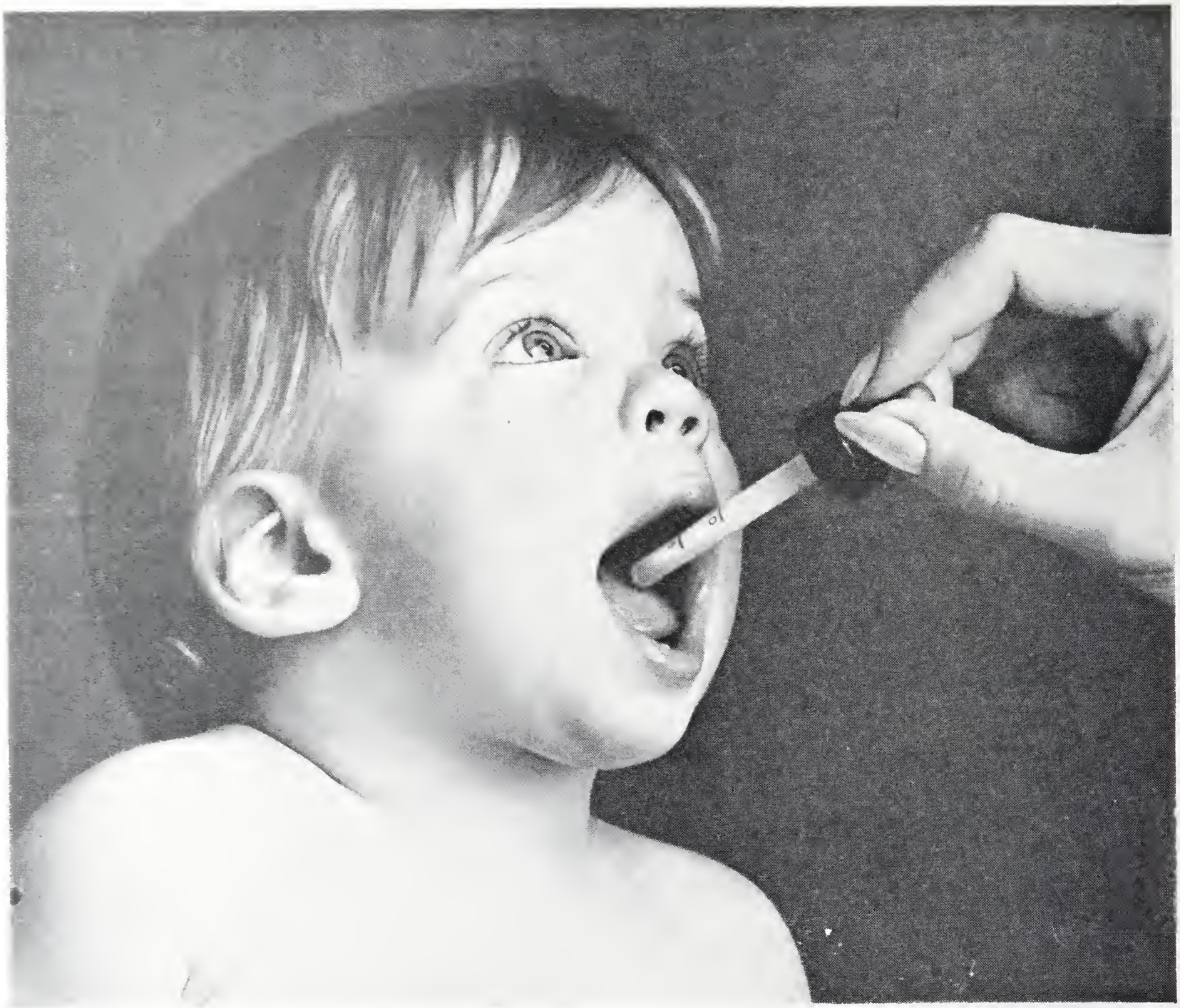
The parenchyma of the brain is insensitive. The principal pain-sensitive structures within the skull are the large blood vessels and sensory nerves and nerve roots. Extracranial arteries are also sensitive and pain may be referred from the eyes, sinuses, teeth, neck or the muscles, ligaments and skin on and around the skull.

19 — D

Pneumococcal meningitis can originate via extension from surface structures or by hematogenous spread. The middle ear, mastoid cells or frontal, ethmoid or sphenoid sinuses are common sites and should always be excluded as the source of infection. In pneumonia, bacteremia may lead to meningitis as it may do in SBE or any other infection with bacteremia.

20 — E

Ruptured intracranial aneurysm almost always presents with the sudden onset of severe headache. Frequently there is loss of consciousness and nausea and vomiting. Because of the irritative effects of blood on the meninges, nuchal rigidity is present. Localizing or lateralizing signs may or may not be present. The clinical sequence of sudden, violent headache, collapse, brief unconsciousness and confusion, combined with an absence of prodromal symptoms and a paucity of lateralizing signs is diagnostic of a ruptured saccular aneurysm or angioma.



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